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DIAGNOSIS OF GALL-BLADDER DISEASE.

By William Fitch Cheney, M.D.,

CLINICAL PROFESSOR OF MEDICINE, STANFORD UNIVERSITY MEDICAL SCHOOL, SAN FRANCISCO, CALIFORNIA.

This paper is based upon experience derived from two sources: (1) from work for twenty years past in medical wards, and (2) from private practice for the same period in internal medicine. But the records of patients seen in wards have been accumulated by various observers, including interns, students and laboratory workers, and, furthermore, are not available now for study; they are therefore excluded from consideration, except as they have influenced the formation of opinions here expressed. All records made in private practice to April, 1906, were destroyed in the fire that swept San Francisco then. During the following thirteen years, from January, 1907, to January, 1920, there were seen for diagnosis and advice 6180 different patients, all of whose records have been preserved. But because the earlier ones of these are not as complete and detailed as the later, only the records for the past eight years have been reviewed as a basis for this study. During this period the total number of patients seen has been 3513, and among these there have been 114 where the diagnosis made was gall-bladder disease.

The methods employed to reach this diagnosis have been the usual ones of history, physical examination, laboratory and roentgen-ray investigations.

I. History. The value of this is so great, especially in all digestive disturbances, that no amount of time spent in eliciting it is ever

wasted. In all these records the history has been taken personally, not through assistants; has been written out in detail, often in the patient's own words; has been revised and supplemented at succeeding interviews, as the case progressed; and has certainly played the most important part in solving the problems presented. But there are numerous variations in the story told by the patient with gall-bladder disease and no one account fits every case. There seem to be four distinct groups, according to history, as follows: *Group 1.* Recurring attacks of colic, with good health between. *Group 2.* Recurring attacks of colic, with more or less constant indigestion between. *Group 3.* Chronic stomach trouble, with subacute gall-bladder attacks. *Group 4.* Chronic stomach trouble, with no history whatever pointing to gall-bladder over long periods of time.

GROUP 1. These are the patients with attacks of biliary colic recurring at irregular intervals, with good health for months or years between. The description they give is usually so characteristic that the story by itself makes the diagnosis. The sudden onset without known cause, the violence of the pain, its site at the right costal margin, its radiation under the right shoulder-blade, its duration for hours at least, all combine to make a picture that is unmistakable. Such a history as the following is typical of this group:

A woman, aged fifty-one years, complains that for the past five years she has had recurring attacks of pain in the upper abdomen. These may come once a month or even once a week, but she has gone two or three months without one. In the interval between attacks she feels perfectly well. The pain comes and ends very suddenly; is felt in the pit of the stomach and across the upper abdomen, radiating to the back, under the right shoulder-blade; its character is colicky and griping; its intensity is very great at times but not always equally so; its duration is very variable but never less than two hours. The attacks bear no relation to food and may precede or follow a meal. During the pain she is nauseated but rarely vomits. After one severe attack distinct jaundice followed. At operation this patient had a small contracted gall-bladder, containing two large stones which completely filled it.

Certain variations of this typical picture may, however, mislead. For instance, the pain may be situated in the epigastrium and radiate straight through to the back, leading to an indefinite diagnosis of indigestion or gastralgia; it may radiate to the left side rather than to the right and so create a suspicion about the heart; it may radiate upward beneath the sternum and thus closely simulate angina pectoris; or it may radiate downward along the right side of the abdomen and so point to the appendix as the site of disease. As regards jaundice, its occurrence as a sequel to the attack of colic makes gall-bladder disease practically a certainty; but its absence

from the story does not throw doubt on the diagnosis when other details are characteristic. Many attacks at their height are accompanied by vomiting, after which the pain subsides; so that the patient is convinced the stomach caused the attack, and this error may be shared by the physician unless he takes into consideration all other parts of the story. But these minor variations in radiation of pain and the presence or absence of jaundice, accompanying stomach symptoms, are all insignificant in comparison with the main features of sudden onset, severity of suffering, site of the pain, repetition of attacks after an interval of good health, and their occurrence unexpectedly, night or day, with no recognizable cause, This history is the most frequent of all in gall-bladder disease, and in this group 45 cases have been recorded out of the total of 114 diagnoses made.

GROUP 2. This group presents not only the story of these recurring attacks of colic but also a complaint of constant stomach trouble between. In fact, the suffering caused by indigestion so obsesses the patient that not infrequently the paroxysms of pain are forgotten in the history unless direct inquiry is made about them. Their features are the same when described as in the cases in Group 1, and the only difference lies in the distressing dyspepsia that fills the intervals between. The following case history is typical of Group 2.

A woman, aged fifty-nine years, complains of spells of what she calls "indigestion" ever since she was twenty: at first coming years apart, but gradually more often, so that now they recur every few months. These spells are characterized by very severe pain, always requiring morphin for relief. This pain comes on gradually and gets worse and worse; is felt in the pit of the stomach, running through to the back; is steady and continuous, not colicky; not accompanied by nausea or vomiting; lasting for hours or until morphin is given; and frequently followed by jaundice for a day or two. In addition to this story she has another of constant trouble with her stomach for twelve years past. She retains her food about three hours, then distress comes on, her stomach grows sour and she has to vomit to get relief because nothing else will give it. She feels better at once after eating, but about two or three hours later her stomach feels too full and burns so that she drinks soda and warm water until she vomits. This condition goes on regularly every day and after every meal and has done so for twelve years. This woman at operation was found to have a small thickened gall-bladder containing one large stone and many small ones.

The manifestations of stomach disturbance are not always the same in gall-bladder disease. Many times the story told corresponds closely to that we are accustomed to attribute to gastric ulcer, because the symptoms are really due to hyperacidity: heartburn,

water-brash, belching, pain, nausea, vomiting, coming on regularly an hour or two after meals. But in other cases the story resembles that found in chronic gastritis and due to hypo-acidity; distress, fulness, sense of weight and distention occurring soon after eating, with persistent belching of gas. The relative frequency of these two varieties of dyspepsia produced by gall-bladder disease will be considered later, when we come to discuss what stomach contents show after a test-meal. But there is nothing about the patient's description of his stomach trouble to identify the gall-bladder as the cause. The evidence that does fix the blame is furnished by the intercurrent attacks of biliary colic, similar in all respects to those described in Group 1. There were 25 cases seen during the past eight years whose history corresponded to the one given in detail for this group.

GROUP 3. The history here varies from both the preceding in that there are no attacks of violent pain. The chief complaint again is of the stomach, and indigestion makes up the main part of the patient's story. But in addition there is given, or can be elicited by questioning, the account of another kind of annoyance or suffering, not so constant but recurring from time to time in "spells." Sometimes the symptoms in these spells amount only to discomfort; sometimes they are more severe; but they never approach in severity or character the typical biliary colic. The location of these manifestations, which the patient recognizes as different from the constant stomach distress, is usually the right side under the ribs, where there is a feeling of fulness and soreness and of something in the way. The following case history presents the story usually told by patients in this group.

A woman, aged sixty years, first seen in January, 1915, complains of stomach trouble she has had for years, characterized by a heavy aching that comes on two or three hours after eating, persisting often until the next meal, with much belching of gas. Her bowels are never constipated but she suffers frequently from diarrhea. The stomach symptoms are nearly constant, the attacks of looseness of the bowels last for several days in every month. Besides these disturbances of health, she describes still other attacks, characterized by dull, aching pain, or "a hurting," as she expresses it, in her right side for days at a time, particularly after getting very tired or after taking a long ride. This pain is never sharp or severe, always dull, aching, annoying and nagging. This patient was found to have complete achylia; was dieted and treated medically at intervals without much benefit; until finally, in April, 1919, she had for the first time in her life an attack of very violent pain, typical of biliary colic, followed by jaundice. She then consented to the operation repeatedly advised during the preceding four years, and was found to have a gall-bladder, with walls greatly thickened and very tough, containing one large round stone.

Other patients in this group tell of a feeling in the right side as if there was "a sore ball" there; of a beating and throbbing and tenderness; or as if something there was going to break because of the sense of fulness; or as if there was something in the way when they bend forward or when they raise the right arm. These symptoms come only at intervals, lasting usually for a day or a few days; but the stomach symptoms are practically constant. The latter are not always the same and there is nothing characteristic about them to identify them as due to gall-bladder disease. This condition is not an unusual one, for there were 34 patients who presented the typical story that placed them in this group.

GROUP 4. There remain certain patients that complain much of the stomach over long periods of time, with no explanation to be found in their history as to the real cause. Sometimes the symptoms they describe correspond to the so-called gastric ulcer type; sometimes to the so-called chronic gastritis type; sometimes a story of gradual loss of weight, in connection with that of chronic dyspepsia, causes suspicion of cancer of the stomach. Frequently in former days these patients were set down as suffering from a "gastric neurosis;" and not infrequently even to this day some of them are labelled with a diagnosis of "achylia gastrica." There are no attacks of biliary colic to direct attention to the gall-bladder, and not even the less serious discomforts described in Group 3. There is really no way to be sure that these cases are due to gall-bladder disease until suddenly, sooner or later, perhaps after the lapse of years, comes a typical attack of severe pain like that described in Groups 1 and 2 to settle the matter definitely; or until, in despair, after trying repeated dietetic and medicinal methods of treatment, without benefit, the patient submits to exploratory operation. That such cases exist, any clinician of experience comes gradually to realize; and though over long periods we cannot reach certainty by any method of diagnosis, we learn to suspect the existence of gall-bladder disease in certain types of history, even though no definite proof is furnished by other methods of investigation. To this group ten cases have been assigned during the past eight years. Others perhaps exist in these records that have been classified under some other name than gall-bladder disease, and that will ultimately reach their proper diagnostic group as development bring out their true nature. A brief *résumé* of the story of several of the cases placed in Group 4 will best show the difficulties of the diagnostic problem.

CASE I.—A man, aged fifty-three years, complains of stomach trouble for about four or five months. He has no appetite and fears to eat because all food causes a feeling of fulness and oppression soon after eating, even while eating. He belches much gas, but has no pain or nausea or heartburn. He has lost twenty pounds since his illness began. His stomach analysis shows complete achylia. Continuing to lose steadily in weight and improving in no respect

on diet and digestive aids, he finally submits to exploratory operation, when the only pathology found is a large single gall-stone, completely filling the gall-bladder. After its removal his symptoms all disappear.

CASE II.—A man, aged forty-two years, first seen in April, 1915, complains of indigestion off and on for the preceding three years. When this occurs he loses his appetite, food causes distress soon after it is taken, he feels too full and distended and belches much gas. He has no nausea or vomiting. He has lost in weight and strength and become very nervous. His stomach also shows complete achylia. The indigestion subsequently continues at intervals in spite of medical treatment, though never sufficient to incapacitate him, until finally, after a Thanksgiving dinner in 1919, he has for the first time after eight years of "stomach trouble" an attack of very severe pain in the upper abdomen, lasting for many hours, with persistent vomiting and followed by jaundice. After this he himself discovers a lump in the upper abdomen the size of a turkey egg, and operation shows a large gall-bladder distended by mucus, the cystic duct blocked by a large stone and many other stones free in the gall-bladder.

CASE III.—A woman, aged thirty-eight years, seen first in February, 1911, complains that she is nauseated nearly all the time, bloats after eating, her food causes heartburn, belching and much gas, but she has no pain and never vomits. She is set down at that time as a case of gastric neurosis, and continues to have more or less similar trouble with her stomach for nearly six years following. Then in December, 1916, begin a series of attacks of very severe pain in the pit of the stomach through to the back, with nausea and vomiting, lasting until morphin is given. Finally, operation in February, 1917, revealed a contracted gall-bladder with thickened walls, containing one large stone.

CASE IV.—A man, aged sixty-two years, complains of stomach trouble present for six months previous. At the outset this was not constant, but lately the stomach never seems right. The appetite is poor and food causes distress, coming on several hours after eating. There is no severe pain every day, but at times it is so severe he cannot sleep, its recurrence depending apparently on what he eats, though any food causes more or less distress. There is much gas and belching. There is no nausea but when a severe spell comes he forces himself to vomit for relief. He has lost about twenty-seven pounds in weight since his illness began. Because of marked hyperacidity found by stomach analysis, and the evidence given by roentgen-ray plates, this man is thought to have duodenal ulcer. He is treated for this and after a month's routine his symptoms all disappear. He remains well for nearly a year, then the symptoms all recur; and this time, after two weeks of gastric disturbance, suddenly comes a typical attack of biliary colic followed by jaundice.

Operation showed the usual thickened and contracted gall-bladder containing two large stones.

Thus in Group 1 of gall-bladder histories, recurring attacks of biliary colic characterize the story, with good health between. In Group 2 stomach symptoms play a prominent part but the colic attacks still form the diagnostic feature. In Group 3 the stomach symptoms preponderate, colic has disappeared and the gall-bladder symptoms have quieted down to minor importance. In Group 4 there are no symptoms but those produced by the stomach, over months or years, and the gall-bladder speaks only vicariously, calling no attention directly to itself. There should really be a Group 5 described where the gall-bladder contains stones, but gives rise to no symptoms of any kind; until either some sudden violent attack of pain, or operation performed for some other ailment reveals cholelithiasis. But these cases sooner or later develop symptoms that put them into one of the four groups described, and they cannot be diagnosed until they do.

II. Physical Examination. In gall-bladder disease this method of diagnosis stands next in value to history, but even so the evidence it gives is very uncertain. The possible results are of three sorts: (1) entirely negative; (2) purely subjective; (3) definitely objective as well as subjective.

1. *Negative Findings.* To anyone who has witnessed operations on the gall-bladder and has noted how far this organ lies beneath the costal margin; furthermore, how small and shrunken the diseased organ is, no surprise is caused by the fact that physical examination so often gives negative results. Nothing abnormal can ordinarily be made out by palpation, during long periods when a diseased gall-bladder is quiescent, even though reflexly it is causing incessant gastric distress.

2. *Subjective Evidence.* Tenderness may be elicited by various manipulations beneath the costal margin, with the patient in different postures; but at the same time no change from the normal be conveyed to the examiner's fingers at all. What the patient feels and the diagnostician does not feel must always be considered with due allowance for individual susceptibilities.

3. *Objective Evidence.* Objective evidence found in gall-bladder disease is of two kinds: (*a*) increased tension and rigidity, and (*b*) palpable tumor.

(*a*) Increased resistance in the right hypochondrium as compared with the left, combined with tenderness on deep pressure there, is the sign we expect to find when cholecystitis is present. But this may not be discovered at one examination and found at another. It is much more likely to be elicited soon after an attack of biliary colic or during the periods of dull ache and sense of fulness described in Group 3. This definite abnormality is probably due to acute exacerbations of a chronic cholecystitis, and disappears again as

soon as the acute inflammation has subsided, so that its absence over long periods of time does not indicate the absence of gall-bladder disease, which may in fact be extensive and advanced.

(*b*) The discovery of a palpable tumor in the gall-bladder area may possibly mean nothing but chronic adhesions about the organ and gall-stones within it. But usually it means more—either an obstruction to the cystic duct with retention of bile or else a neoplasm. It is a law of clinical medicine, long ago announced by Courvoisier and since confirmed by many observers, that in chronic jaundice due to obstruction of the common duct by a gall-stone the gall-bladder is small, while in chronic jaundice due to neoplasm the gall-bladder is distended. This law is based upon the fact that chronic cholecystitis and cholelithiasis make the gall-bladder small, thickened and contracted; and if on physical examination a tumor is palpable with or without jaundice, the conclusion is therefore justified that something unusual has been added to the clinical picture, and that there exists distention of the gall-bladder by accumulation of bile and mucus within its cavity or else neoplasm that has developed in its walls. But as these conditions are unusual so ordinarily no tumor is palpable in gall-bladder disease.

III. Laboratory Examination. No diagnostic evidence is furnished by blood counts in gall-bladder disease. The urine may be dark in color and show bile, while the feces are light in color and show deficient bile, during or shortly after an attack of biliary colic, even though the skin and conjunctivæ are not noticeably yellow. But urine and feces convey no information of diagnostic value in gall-bladder disease except at the time of such emergencies. As regards direct examination of bile obtained by duodenal tube, as described by Einhorn, Rehfuss, Lyon and others, attempts have been made in this series of cases to employ this method, but not with satisfactory results. The objections found have been with the practicability of the method not with its value; but this value has not been found so great as to offset the obstacles offered in securing duodenal contents and in getting them properly examined chemically, microscopically and biologically.

As regards stomach analysis, it tells us when abnormalities in secretion exist but nothing as to their cause; and there is no type of abnormality absolutely diagnostic of gall-bladder disease. In the series of cases reviewed, gastric analysis was made 81 times. With stomach contents removed forty-five minutes after the Ewald test-meal and assuming the normal range of total acidity to be 40 to 60, the results found were as follows: total acidity under forty in 26 cases and under twenty with complete absence of free HCl in 12 of these; total acidity over sixty in 38 cases; all the other seventeen analyses within normal limits. There were therefore more patients found with hyperacidity than with hypo-acidity in this series. From experience acquired not only in these gall-bladder cases but in many

other gastric disorders from which these have been sifted out the truth seems to be as follows: gall-bladder disease may be associated with either hyperacidity or hypo-acidity; but while hyperacidity is found as frequently with ulcer or chronic appendicitis as with gall-bladder disease, hypo-acidity, and particularly achylia, is found with gall-bladder disease more often than with any other pathology except cancer. Therefore the discovery of achylia with a dubious history of chronic stomach trouble, as in the cases in Group 4, adds much to the suspicion that disease of the gall-bladder is the underlying cause.

IV. Fluroscopy and Roentgen-ray Plates. Much information of great value is supplied by this method of diagnosis in gall-bladder disease; nevertheless, it may in a given case add nothing to the facts already collected by other means, and, on the other hand, the testimony it gives may appear to implicate the gall-bladder when no disease is there. The evidence obtained by this method of investigation is of three kinds: direct, indirect and eliminative. (1) Direct evidence means the demonstration of changes in the gall-bladder itself, either the shadow of its outlines or of stones within it. But these findings are unfortunately not the rule even when other evidence is conclusive. A liberal estimate seems to be that one-half the cases of gall-bladder disease give such direct signs by means of the roentgen ray, and possibly this estimate should not be more than one-quarter. (2) By indirect evidence is meant demonstration of effects produced on other surrounding parts by the gall-bladder disease, such as flattening or deformity of the duodenal cap; pulling of the stomach to the right, or a high position and fixation of the hepatic flexure of the colon. But all of these signs are caused by pericholecystitis, leading to adhesions between the gall-bladder and adjacent organs, and as pericholecystitis does not always occur, even with long-standing gall-bladder disease, none of this indirect evidence may be found. (3) By eliminative evidence is meant the exclusion of other pathology possibly causing the history and physical signs and disturbances of stomach function. It greatly simplifies the diagnosis in certain cases to have positive demonstration by fluoroscope and by roentgen-ray plates that no cancer or ulcer exists at the pylorus or in the duodenum; that no changes are found to indicate disease about the appendix or cecum; that there is no break in the continuity of the colon and no marked ptosis of stomach or bowel. These negative findings are certainly of great value and justify the investigation even though no positive signs are found that point to gall-bladder disease.

But interpretation of what is shown by fluoroscope and by roentgen-ray plates is always open to error and must not be accepted as final when it disagrees with evidence obtained by other means. For instance, in several of the cases reviewed in this series, with

most positive history pointing to gall-bladder disease and with gall-stones subsequently found at operation, the roentgen-ray report was entirely negative, no direct or indirect evidence being furnished of the condition present. Again, with chronic gastric disturbance due to hyperchlorhydria as shown by gastric analysis, with no history pointing to gall-bladder disease, and with much depending on roentgen-ray examination to throw some light on the pathology present, the report comes back of a deformed duodenal cap leading to a diagnosis of ulcer. But ultimately an attack of biliary colic justifies a revision of this diagnosis, and at operation the deformity of the duodenum is proved to be due to adhesions. Great, therefore, as is the value of roentgen-ray evidence, it must be remembered that it is not infallible, and its testimony must not be accepted as unassailable.

Such are the methods by which we recognize the presence of gall-bladder disease. There are not many forms that this presents. Probably cholecystitis is always the first phase, and this must exist for a variable length of time before gall-stones are added and the condition becomes cholelithiasis. Theoretically we ought to be able to distinguish one from the other, but practically we are not; and, after all, it makes no great difference, for a diseased gall-bladder needs to be removed whether it does or does not contain stones. When a stone becomes lodged in the cystic duct and the gall-bladder consequently distended because its outlet is blocked, an elastic tumor forms that is easily palpable and usually can be recognized without difficulty. If a hard tumor is found instead, whether smooth or irregular, suspicion should be aroused at once of cancer. But here again differential diagnosis should not take up much time, because either condition calls for surgery as promptly as possible after a tumor is discovered. As it is difficult to decide where cholecystitis ends and cholelithiasis begins, so it is equally difficult to tell where cholelithiasis ends and cancer begins. We have no methods, unfortunately, for the recognition of malignant degeneration of the gall-bladder before a palpable tumor has formed, and then it is usually too late for the surgeon to successfully remove it, because of metastases.

In conclusion, history seems to be the most valuable aid in the recognition of gall-bladder disease. When this is characteristic, as in Groups 1 and 2, it makes the diagnosis, no matter whether or not at a given time signs are found by physical examination, no matter what the stomach analysis shows, no matter whether the roentgen-ray report does or does not present any direct or indirect evidence. When the history is less characteristic, as in Group 3, it still remains the most important factor in diagnosis; but physical examination comes next in value and may give signs that with the history serve to remove all doubt, regardless of laboratory and

roentgen-ray reports. When we come to Group 4 history alone makes us only suspect, and we need all the clues we can get from physical signs, secretory disturbances and roentgen-ray shadows to enable us to pass beyond suspicion that the gall-bladder is diseased. Without enough collateral evidence to supplement deficient history in this group we cannot reach certainty, and so we usually wait for months or years, indefinite and undecided, until at last it is history that settles the matter by introducing an attack of biliary colic. Thus we come back in the diagnosis of gall-bladder disease to old and well-tried methods as the most useful; to careful and painstaking history and to such facts as we can elicit by the unaided senses—by sight and by touch particularly. We do not neglect any possible laboratory or instrumental aid, but we place most reliance on what the patient tells us and on what we see and feel for ourselves.

INVOLVEMENT OF THE AURICLE AND CONDUCTION PATHWAYS OF THE HEART FOLLOWING INFLUENZA.[1]

By Walter W. Hamburger, M.D.,
CHICAGO, ILL.

(From the Electrocardiographic Laboratory, Michael Reese Hospital, Chicago.)

During the past year a number of interesting postinfluenzal cardiac conditions, late results of the 1918 influenza epidemic and more recent complications of the epidemic of 1920 have been observed and studied in the electrocardiographic laboratory of the Michael Reese Hospital. Certain of these cases throw light on the mode and site of action of the influenza poison on the cardiac mechanism, particularly on the auricle and conduction system, and clarify, to some extent, the more general statements of observers in the earlier epidemics. It is for this reason that the following cases are reported.

A number of suggestive studies have already appeared, Lucke, Wight and Kime[2] from a detailed study of necropsies from 126 definitely proved fatal cases of influenza, concluded that in the majority of instances acute parenchymatous changes of the myo-

[1] Read at the Meeting of the Association of American Physicians, Atlantic City, May 4, 1920.

[2] Pathologic Anatomy and Bacteriology of Influenza, Arch. Int. Med., 1919, xxiv, 154.

cardium, similar to the changes of other acute infectious diseases, occurred. In over 90 per cent. of these cases more or less relaxation of the right heart was present; in over 88 per cent. an associated cloudy swelling occurred. Microscopically they found acute parenchymatous degeneration and vacuolization. While these cases represented the fatal ones it may be inferred that in the less seriously ill patients the heart is similarly affected, though to a less degree.

Other reports, although not as conclusive as the above, admit some degree of myocardial involvement. For example, Hart,[3] although believing that the cyanosis and death in influenzal bronchopneumonia is not primarily cardiac in origin, admits that in the few uncomplicated cases in which the heart was carefully studied a moderate degree of myocardial degeneration was found. Smith,[4] in a study of postinfluenzal tachycardias at Camp Travis, concluded that organic heart disease was not the basis of the tachycardia and quotes various autopsy reports from army camps as to the infrequence of myocardial involvement, judged largely from gross appearances. Later, however, he states "It is possibly true that pathologic changes, sufficient to cause serious disturbances in later life, could have easily been overlooked with the naked eye."

A somewhat similar conflict between clinical and necropsy findings may be found in Sir James Mackenzie's discussion of "Cardiac Complications of Influenza,"[5] wherein he states that "if one looks at the heart postmortem in these fatal cases one sees the extensive damage done to the myocardium," and continues, "It is possible that influenza may lay the beginnings of a myocarditis which ultimately leads to heart failure, but I have not seen this occur in the many cases I have met in general practice." He concludes, in reference to the late effects: "The weakness after influenza is not, properly speaking, cardiac in origin, but is the outcome of an injury to other systems as well as the heart, such as the central nervous system. Even when we find such marked abnormalities as increased rate, systolic murmur, increase of size of heart and extrasystoles the cause of these signs ought not to be looked upon as heart disease, but merely as manifestations of general illness." In reference to the effect of influenza on patients with chronic heart disease, Mackenzie states, "I never found that influenza injured them in any way. Everyone, even those with advanced heart failure, passed through the attack scathless."

Thomas Lewis,[6] however, takes issue with Mackenzie in the follow-

[3] The Heart in Bronchopneumonia: Observations on the Activity of the Heart and its Response to Digitalis Made during the Recent Epidemic, Am. Jour. Med. Sc., 1919, clviii, 649.

[4] Tachycardia Following Influenzal Pneumonia, Jour. Am. Med. Assn., 1919, lxxiii, 1685.

[5] Cardiac Complications of Influenza, Practitioner, 1919, cii, 19.

[6] The Soldier's Heart and the Effort Syndrome, New York, 1919.

ing words: "The relation of infection to the cases of real heart disease must also be emphasized. It is of first importance. Nothing jeopardizes the condition of a heart patient more than infection, be the infection rheumatic fever or infection expressed as tonsillitis, influenza, bronchitis, etc. During the recent influenza epidemic the infection spread to a ward reserved for cases of serious heart disease. We lost two patients, and the lives of several others were seriously jeopardized."

These several studies are sufficient to emphasize the diversity of opinion regarding the effects of influenza on the heart, notwithstanding which some degree of uniformity of opinion is beginning to crystallize and may be expressed as follows:

1. Necropsies of fatal cases of influenza, in spite of slight gross pathologic changes in the heart, show rather universally acute parenchymatous degeneration and vacuolization, and, at times, extensive myocardial damage. Group I.

2. Clinical studies during the acute stage of illness, and in convalescence, indicate a rather remarkable recoverability of complete cardiac function. The postinfluenzal flabby heart muscle gradually disappears under graduated and properly directed exercise. Several of our cases are of this type. Group II.

3. Certain of these acute myocardial processes, however, do not clear up, at any rate for a very long time, and become cases of true postinfluenzal myocardial insufficiency. The present cases for the most part fall into this last group. Group III.

A very few electrocardiographic studies in influenza have appeared. Cockaynes'[7] description of heart-block and bradycardia is of special interest in this connection. He found that simple bradycardias were caused by a poisoning of the myocardium, especially the sino-auricular node; the cases of heart-block result from the poisoning of the muscle of the auriculoventricular bundle; while two cases of marked bradycardia with prolonged *A–V* interval were due to the involvement of both sino-auricular and auriculoventricular areas. He reports one boy, aged sixteen years, with sinus block, who had a mild right-sided postinfluenzal pneumonia that cleared up entirely in twenty-eight days. The prolonged *A–V* ("P–R") cases appeared in mild pneumonias and lasted from nine to twenty-three days. Nine cases of two to one heart-block were observed, lasting from one to thirty-three days. Six cases of three to one heart-block averaged fourteen days. The onset of the bradycardia usually occurred after the temperature had become normal. Most of the patients were young men suffering from mild influenzal pneumonia. After six weeks only one complained of cardiac symptoms. None showed any undue irritability of the heart.

[7] Heart-block and Bradycardias Following Influenza, Quarterly Jour. Med., 1919, xii, 409.

CASE I.—S. R., teamster, aged twenty-five years, married, entered the hospital August 20, 1919, complaining of moderate shortness of breath and precordial discomfort varying in intensity, necessitating, at times, rest in a recumbent posture. He was in robust health up to April, 1919, at which time he had a moderately severe attack of influenza, with temperature 101° to 102°. Against

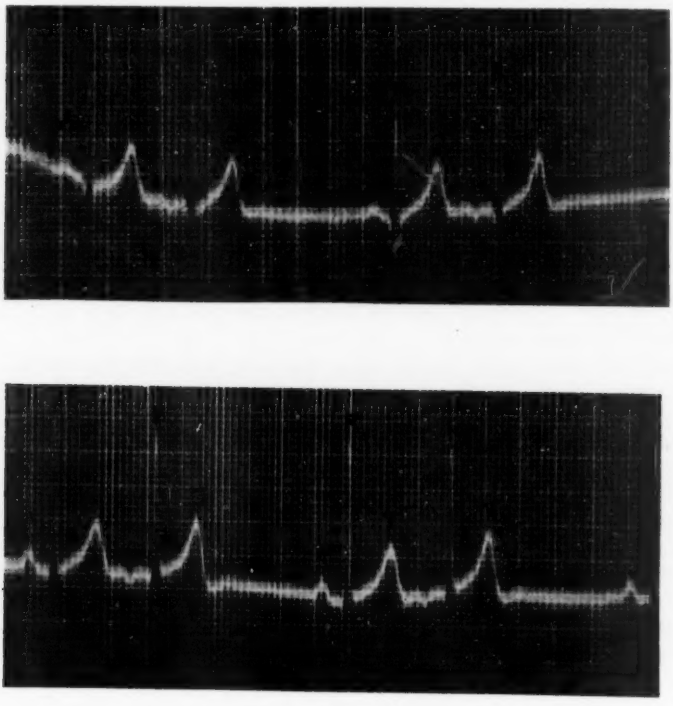

FIG. 1.—Case I. S. R. Postinfluenzal myocarditis. Pulsus bigeminus caused by regularly recurring auricular extrasystoles—ectopic—(inverted) auricular contractions (P_2) following normal contraction of the auricle (P_1).

the advice of his attending physician he remained home only three days, returning to his work as a teamster while not entirely free from fever. Two weeks later the above complaints occurred. He is a moderate smoker. Examination of his heart shows the apex in the fifth interspace, the left border 10 cm. the right 4 cm. from the midsternal line. Heart tones irregular, occurring in groups of two, pulsus bigeminus, no murmurs. His systolic blood-pressure was

115 mm. Hg, diastolic 55 mm. Hg. The urine was negative, blood negative and blood-Wassermann negative. Electrocardiographic examination showed a pulsus bigeminus due to regularly recurring auricular extrasystoles, "P" being inverted, "ectopic," every second auricular beat (Fig. 1). At the present (April, 1920), one year after his influenza infection, patient is able to take care of a small newsstand, to which occupation he was advised to change because of inability to work as a teamster. Recent examination

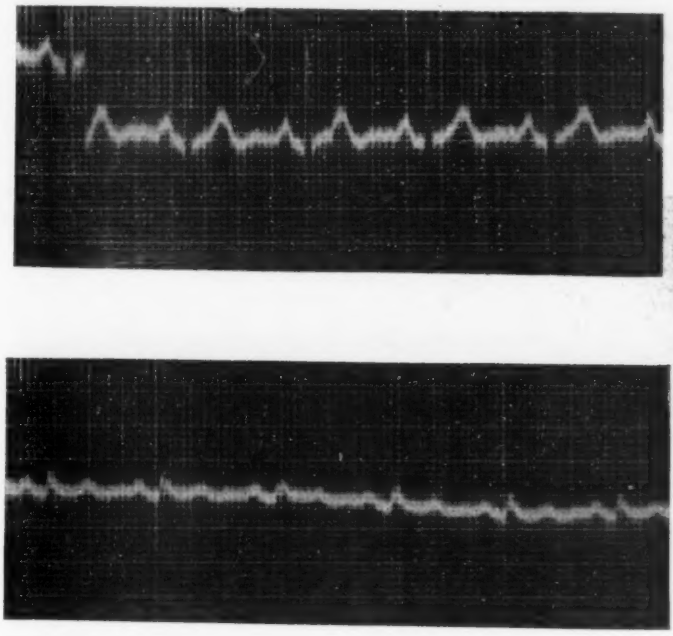

FIG. 2

at the dispensary showed a perfectly normal pulse when at rest, which, however, promptly changed to bigeminus following slight exertion, sitting up and lying down, on the examining table. Summary: Postinfluenzal auricular myocarditis, pulsus bigeminus, auricular extrasystoles. Group III. Duration twelve months.

CASE II.—Dr. S., Mobile, Alabama, aged thirty-eight years, physician. He entered the Medical Reserve Corps of the army in June, 1918. In October he had a moderately severe attack of

influenza, without pneumonia, but with complicating frontal sinusitis. Since the influenza he has noticed a slight dyspnea, particularly on playing golf. He believes his endurance low and notices

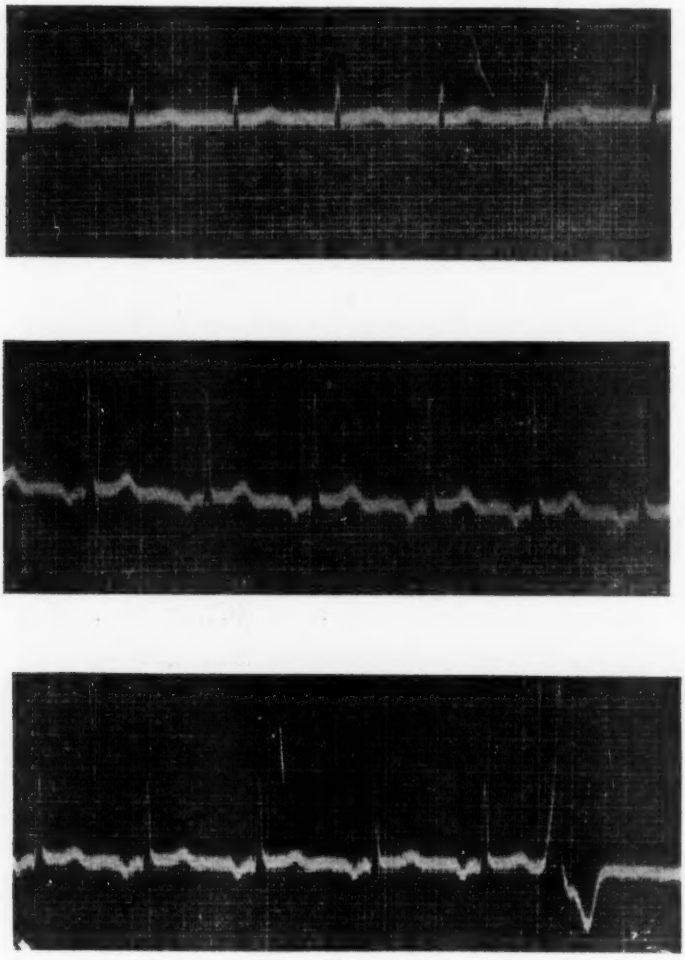

FIG. 3

that he tires easily. When previously he was able to work without fatigue from seven in the morning to twelve at night he now scarcely can get through his day from eight in the morning to three in the

afternoon. He still complains of frontal headache. There is no precordial pain or edema of the ankles. His systolic blood-pressure is 150 mm. Hg, diastolic 90 mm. Hg. His right heart measures 3 cm., his left 11½ cm. from the midsternal line. The pulse was 88, the heart tones regular and clear; there were no accentuations or murmurs. Immediately after exercise his pulse increased to 132, after two minutes to 128, after five minutes to 112 and after ten minutes to 100. His urine showed two plus albumin, microscopic negative; leukocytes 6800. The electrocardiographic examination showed "P" high in L. I, II. and "R" low and notched in L. III. (Fig. 2). Diagnosis: In view of the poor response to effort, marked fatigue, dyspnea, albuminuria and electrocardiographic findings a diagnosis of postinfluenzal myocardial insufficiency. Group III. Duration fourteen months.

Case III.—C. H. W., aged thirty years, merchant, had a mild attack of influenza in September, 1918, and a recurrence in November, 1918. In neither attack, although there was a rise of temperature, did he take to his bed. Following the last attack he noticed a marked loss of endurance and an irregularity of his pulse. Examination of his heart was entirely negative except for an occasional extrasystole before exercise at long intervals. Exercise tests (hopping fifty times on one foot) showed a pulse of 93, systolic blood-pressure 122 mm. Hg, diastolic 75. Immediately after exercise the pulse was 126, systolic pressure 135, diastolic 65. Two minutes after exercise the pulse was 95, systolic pressure 118, diastolic 65. Electrocardiographic examination (Fig. 3) shows absence of "P" in L. I. and inversion of "P" in leads 2 and 3, extrasystole of right ventricular origin in L. III. Diagnosis: In view of fatigue not felt before the attacks of influenza, extrasystoles and electrocardiographic findings a diagnosis of postinfluenzal auricular and ventricular involvement was made. Summary: Postinfluenzal, right ventricular extrasystoles and "ectopic" auricular contractions. Group III. Duration fifteen months.

Case IV.—Dr. B., aged twenty-eight years, house physician, entered the hospital March 3, 1920, complaining of sore-throat, with a history of attendance on several nurses who had been on duty in the influenza wards and who had become ill, suffering with sore-throat, temperature and generalized pain. Dr. B. complained of pain in his knee-joints, palpitation, sensation of "heart stopping," moderate frontal headache and nasal discharge containing pure Streptococcus hemolyticus. The past history revealed the usual exanthemata of childhood and a moderately severe attack of rheumatism of three weeks' duration following sore-throat seventeen years ago. The mother died of a cardiac lesion at the age of thirty-

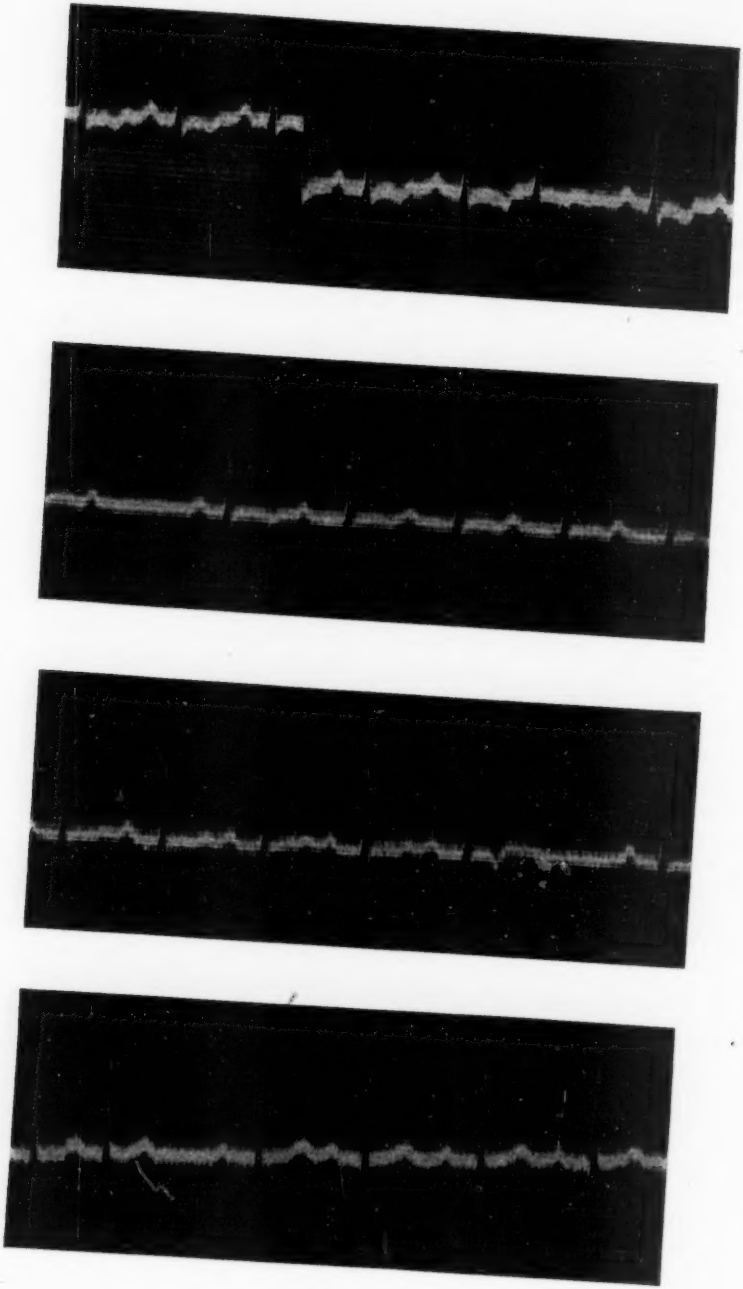

FIG. 4

three. The father had attacks of rheumatism. Examination showed a large, well-nourished, obese young man, lying quietly in bed without evidence of respiratory or cardiac embarrassment, with purulent nasal discharge. Examination of the heart showed no evidence of gross circulatory failure. The pulse-rate was seventy, with an intermittence about every thirty beats. The quality was soft and compressible, the apex fifth interspace, feeble, no thrill. The left border was inside the nipple line, the right border at the right sternal margin. The heart tones were soft and there was no murmur. There was no edema of ankles. March 4 the pulse was irregular and there was some swelling of the knee-joints and small joints of the feet. The electrocardiographic report (Fig. 4) showed moderate left preponderance, diphasic "P" in lead I, and auricular extrasystoles. P–R. .20, rate 109.

Electrocardiogram March 16 (Fig. 4) shows auricular extrasystoles, dropped beats, P–R .32 to .36. Rate 96. Progressive lengthening of P–R.

Electrocardiogram March 22 (Fig. 4) shows the blocking of an auricular extrasystole. P–R .24, rate 88.

Electrocardiogram March 26 (Fig. 4) shows P–R, averaging .24, pulse 90, auricular extrasystoles arising in the neighborhood of sinoauricle node. P. T. Superimposed. Electrocardiogram, April 20, shows normal cardiac mechanism.

Summary and Diagnosis: Acute streptococcus myocarditis involving particularly the auricle and conduction pathways producing chronologically, ectopic auricular extrasystoles; involvement of the auriculoventricular bundle with delay in the P–R interval and occasional dropped beats (early heart-block); blocking within the auricle of ectopic extrasystoles; auricular extrasystoles arising in the immediate neighborhood of the sinoauricular node. Group II. Duration six weeks.

Case V.—Miss E. S., pupil nurse, aged twenty-three years, entered the hospital March, 1920, complaining of sore-throat and loss of weight. Since a septic sore-throat December 19, 1919, containing hemolytic streptococcus, she had had more or less throat infection and felt weak on slight exertion and tired easily. Examination showed the hands and face to be very pale, anxious facies, apparently suffering, hands held over the heart, respirations shallow and superficial, pulse 114. She complained of gripping pain over the heart that made speech and breathing difficult. She said that she could feel her pulse become slow and irregular, after which attacks the pulse became more rapid. There was a marked tenderness in the fifth interspace. The apex lay within the nipple line in the third and fourth interspace. The heart tones were irregular. There were no murmurs. An electrocardiogram taken

March 3 (Fig. 5) showed a three to two heart-block, rate 62 of the ventricle. An electrocardiogram taken the following day showed nodal rhythm, rate 89.5 (Fig. 5).[8] March 9 the heart seemed normal,

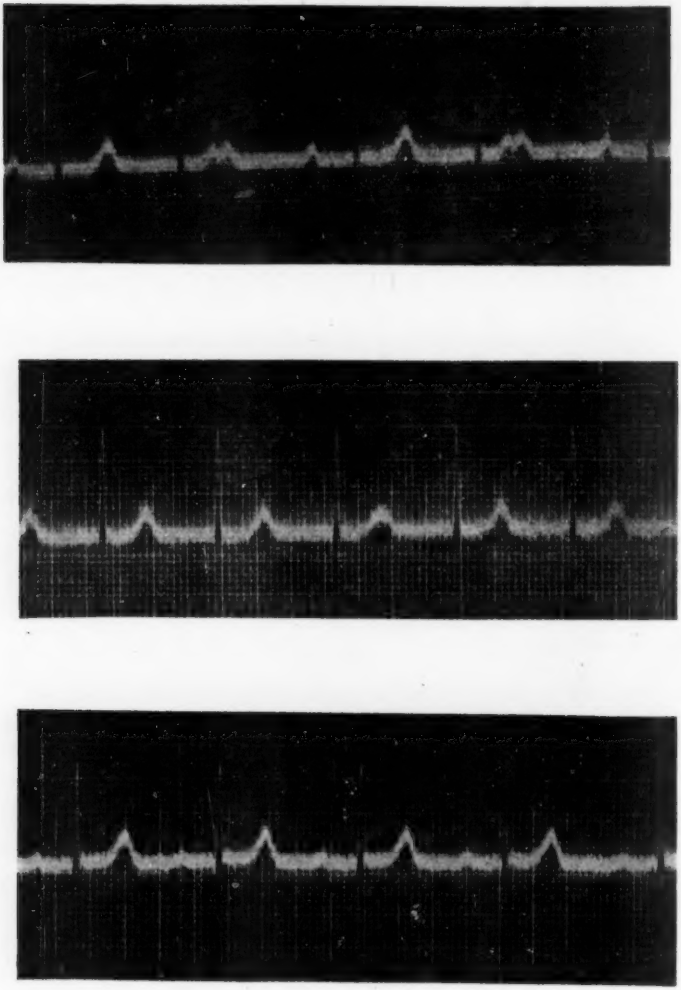

FIG. 5

[8] Dr. Robinson, who kindly looked over this curve, believes it more likely markedly delayed P–R interval with P buried in the T complex.

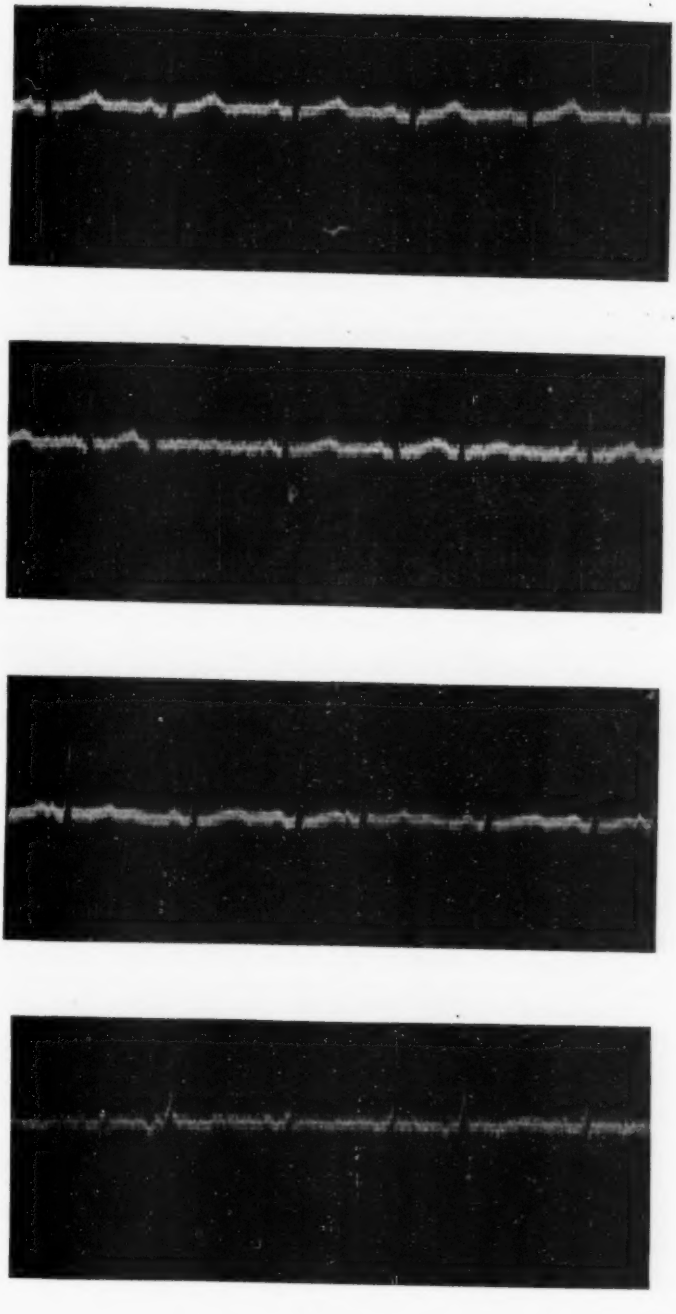

Fig. 6

there were no accentuations and the first sound was barely perceptible. The electrocardiographic examination showed P–R .25, rate 65.2. One week later examination showed normal cardiac mechanism. Summary and diagnosis: Acute streptococcus myocarditis involving primarily the bundle with three to two partial heart block, later nodal rhythm, with anginal attacks. Group II. Duration two weeks.

CASE VI.—Miss H. N., stenographer, aged twenty-eight years, has had "heart trouble" since the "flu" in October, 1918. Remained in bed three weeks during attack; there were no lung complications, but some cardiac irregularity during acute illness. Remained home two months convalescing. In the spring of 1919 complained of same precordial uneasiness with slight pain, relieved partially by digitalis.

January, 1920, again complained of pain in heart region; no dyspnea or pain with effort; some palpitation. At times has some throbbing sensation in left arm. Has lost six pounds past few weeks, tires easily, gets extremely fatigued.

Past Illnesses. Scarlet fever eight years ago. Inflammatory rheumatism at twelve years of age in knees and elbows; recurring tonsillitis; tonsillectomy five years ago.

Examination. Right heart 3½ cm. left 12 cm. midsternal line. Arrhythmia (extrasystoles) left border just outside nipple line.

Electrocardiograph. Auricular extrasystoles in all leads arising in neighborhood of pacemaker, number possibly increased after atropine.

Summary. Chronic postinfluenzal myocarditis, with localization in the auricle, resulting in auricular extrasystoles. Duration seventeen months. Group III.

Discussion. The above cases, cited as examples from a larger group, are offered as evidence that the acute epidemic respiratory infections known as influenza, cause damage to the cardiac mechanism, which may be demonstrated clinically and electrocardiographically. As observed by the latter method these infections affect, for the most part, the auricle and conduction pathways of the heart, although clinically it may be supposed that ventricular involvement also occurred. Unfortunately no gross or microscopic pathologic material was available for study. Cases IV and V, in which hemolytic streptococci seemed to be the predominant etiologic organisms, are strikingly similar to Cockayne's cases of influenzal poisoning of the sino-auricular node and auriculoventricular bundle, thereby substantiating the influenzal involvement of the auricle and the His bundle.

One feels justified in concluding that at least in a certain percentage of cases, acute influenza (streptococcus) picks out early and to a degree exclusively the auricle and conduction pathways.

Barker's[9] recent interesting case of arrhythmia with auricular involvement following focal infection may still further broaden our views as to the general point of attack of infectious agents and poisons on the cardiac mechanism.

Conclusions. 1. Six cases of postinfluenzal myocardial involvement are reported, involving particularly the auricle and conduction pathways of the heart.

2. From a survey of the literature together with clinical and electrocardiographic studies, a grouping of postinfluenzal cardiac complications is offered as follows:

(*a*) Fatal cases showing acute parenchymatous degeneration and vacuolization of the myocardium.

(*b*) Non-fatal, acute cases, showing involvement of auricle and conduction system during height of infection, with complete restoration to normal cardiac mechanism with subsidence of infection. Duration two to six weeks.

(*c*) Non-fatal chronic cases with arrhythmia and involvement of the auricle persisting and causing partial invalidism long after subsidence of acute infection. Duration twelve to seventeen months—plus.

3. Suggestion is offered that acute respiratory infections (Influenza, Streptococcus) single out early the auricle and conduction pathways of the heart.[10]

Appreciation to several members of the Hospital Staff is herewith offered, for permission to publish curves of their cases, and in particular to Miss Marguerite Collver, laboratory technician, for invaluable aid in the preparation of this material.

DETERMINATION OF THE NEED OF SURGERY IN PEPTIC ULCER, WITH REMARKS ON GASTRO-ENTEROSTOMY.[1]

By W. A. Bastedo, M.D.,

ASSISTANT PROFESSOR OF CLINICAL MEDICINE, COLUMBIA UNIVERSITY; ATTENDING PHYSICIAN, CITY HOSPITAL, NEW YORK; ASSOCIATE ATTENDING PHYSICIAN, ST. LUKE'S HOSPITAL.

A study of surgical statistics would convey the impression that in operative procedure we have a dependable cure for gastric and duodenal ulcer; and last year before this Association, Alvarez said: "My own conviction after many years of seeing these ulcer patients

[9] Cardiac Arrhythmias, Arch. Int. Med., 1919, xxiii, 158.

[10] Probably the infections affect the whole heart similarly (*cf.* microscopic studies of auricle and ventricle), but due to other factors, such as thinness of the auricular wall, presence of ganglion cells or other unknown conditions, disturbances of auricle and conduction pathways first become evident.

[1] Read before the American Gastro-enterological Association, May 4, 1920.

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returning with relapses is that our medical treatments do little if any good except in rare cases." Yet in our own practice ulcer cases that have had one or more operations come for treatment almost as frequently as ulcer cases that have not been operated upon; and other gastro-enterologists tell us that this is also their experience. Such antagonistic ideas, therefore, furnish our excuse for this presentation on a somewhat hackneyed subject.

Ulcer cases may require emergency treatment or they may not, and this fact divides them into two groups.

I. The Emergency Cases. The two striking emergencies which occur in gastric and duodenal ulcer are acute perforation and profuse hemorrhage. In acute perforation all will agree the earliest possible surgery is imperative.

In serious hemorrhage, on the other hand, it is generally the opinion that operative intervention is dangerous and mostly futile. Sir Berkeley Moynihan, in issuing a warning against hasty surgery, estimated that not more than 3 per cent. of profusely bleeding gastric and duodenal ulcers could be treated successfully by laparotomy. Lindberg, of Copenhagen, tabulated 68 cases of hematemesis so severe as to raise the question of an emergency operation. In all of the 68 surgery was decided against. Five died, and at autopsy it was found that not one of these could have been helped by surgery. On comparing these statistics with others from clinics where operation had been the choice, Lindberg was convinced that surgical measures are never indicated in cases of acute hemorrhage from the stomach or duodenum. We find that many surgeons have had the trying experience of opening a stomach in such a case and being unable to find the site of the bleeding. Lund, of Boston, said: "I have learned that it is poor practice, when the patient is depleted by hemorrhage, to open the stomach and try to grasp the artery in the bottom of an ulcer." Other surgeons speak in like manner.

Yet now and then one hears of a case in which life has undoubtedly been saved by surgery, as where perforation accompanied the hemorrhage or where the bleeding-point was readily found. We have in mind a recent case where a vein was held open by the indurated tissues and where undoubtedly death would have ensued had operation not been performed. And it is a trying experience, and one that seems inconsistent, for a physician to stand helplessly by while a patient vomits copious amounts of blood every hour or two and rapidly becomes exsanguinated under his very eyes. The dificulty lies in the fact that as these hemorrhages mostly cease spontaneously and are not fatal we prefer to wait, and then when we decide that the bleeding probably will not stop it is too late for surgery.

In any case, therefore, while applying the proper medical measures we should, when possible, prepare for transfusion. If the bleeding persists transfusion is the measure of choice. If transfusion fails

to stop the bleeding it at least puts the patient in better condition for surgery, which then, in our opinion, might be resorted to. Thus very few of the cases would come to surgery, but these few, being hopeless otherwise, might include a sufficient proportion of operable cases to justify the procedure. That is to say, the great risk of operative intervention and the small chance of helping by operation are overshadowed by the almost certain supervention of the patient's death if operation is not performed. In such a case the surgeon who fails is without blame.

II. Cases not in the Emergency Class. In the treatment of an ordinary ulcer case surgeons are not now so ready to operate as formerly, and many grant that judgment is required as to the need of surgery; for operation always produces a damaged abdomen and a damaged stomach with a new anatomy and a new physiology; it is followed only too often by undesirable sequelæ; and frequently enough it leaves the patient relieved for a time, only to have him return later with a recurrence of symptoms which, because of the surgical damage, may be more difficult to treat than before. As Connell expresses it: "The immediate result is invariably most encouraging, but relapse is far from uncommon."

We cannot here discuss the merits of the various surgical procedures, nor compare one with another, but because it is the usual operation we shall dwell briefly on the subject of gastro-enterostomy, referring you for much interesting data to the papers of Dr. Frank Smithies and Drs. Wilensky and Crohn, which have been read recently before this Association.

Gastro-enterostomy. "This operation," in the words of Frank Martin, "has been for years the cure-all for almost every stomach malady that exists." Of 261 ulcer cases returning for treatment after operation, Smithies found that gastro-enterostomy had been done in all. But among the best surgeons today it would seem to be considered of value only for ulcers of the duodenum and of the pyloric and antral regions, and not, except in rare cases, for ulcers in the body of the stomach or high up on the lesser curvature. Indeed, many eminent surgeons agree with Deaver that "when the ulcer is located elsewhere than at the pyloric end posterior gastro-enterostomy does little if any good." However, Mills has directed attention to the fact that in certain hypotonic types of stomach, after a V-shaped or sleeve resection for ulcer of the lesser curvature, a gastro-enterostomy is required; we also have seen the necessity for gastro-enterostomy in just such cases and Peck has expressed the opinion that it is a wise procedure. Sir Berkeley Moynihan has said "under no circumstances is the operation to be done in the absence of demonstrable organic disease." Yet this cannot be an absolute rule for we have had good results in a few rebellious cases of marked gastric atony without ulcer.

Among the various reasons advanced in surgical writings to justify

simple gastro-enterostomy those usually met with are the following: (1) That it relieves the pyloric end from muscular activity and from the irritation of food and gastric juice; (2) that it relieves the pyloric end from high peristaltic pressures; (3) that by being placed at the most dependent portion of the stomach it favors gravity drainage; (4) that it favors stomach emptying regardless of gravity drainage; (5) that by permitting the alkaline duodenal contents to flow back into the stomach it decreases gastric acidity. Let us consider these seriatim:

1. *That it Relieves the Pyloric End from Muscular Activity and from Food and Gastric Juice.* To emphasize the stress laid upon this factor, I would quote Richard Lewisohn, who wrote as late as 1918: "Even at the present day many surgeons consider gastro-enterostomy a safe procedure to keep food material away from the ulcer-bearing area." In the majority of cases the ulcer-bearing area is the antral, pyloric or duodenal region. Without giving the data in detail I might say that it has been shown repeatedly, both by laboratory experiments and by the roentgen rays (see 4 below), that after a gastro-enterostomy peristaltic waves occur in the pyloric end of the stomach the same as before the operation; that to a certain extent and sometimes in their entirety the food and gastric juice are swept past the new opening and take their normal course to the pylorus; and that vigorous churning takes place in this end of the stomach. In 262 postoperative cases Smithies found chymification after a mixed meal good or fair in 90 per cent. Therefore we may say that gastro-enterostomy does not result in relief of the pyloric end from muscular activity or from the irritation of food and gastric juice, though it probably lessens the degree of these.

2. *That it Relieves the Pyloric End from High Pressures.* It is at the antral and pyloric regions that normally intragastric pressure rises to the highest point. Moritz found the intragastric pressure at the cardiac end 6 to 8 cm. of water, and at the pyloric end 20 to 30 cm., with rhythmic rises to as high as 60 cm. Sick found the cardiac pressures 6 to 16 cm. and the pyloric pressures 25 to 42 cm., and von Pfungen, in a boy with a fistula in the midstomach, found the maximum pressure at the fistula 19 cm. and that at the pylorus 162 cm. In ulcer cases with hypermotility the pyloric pressure is probably quite high and in cases with hypermotility and pyloric obstruction, whether organic or spasmodic, the pyloric and antral pressures probably rise very high indeed. In pyloric obstruction without atony Crohn and Wilensky have shown that the hunger contractions may take on a spasmodic character, with correspondingly high intragastric pressures, a condition abolished by operation. They found that except in these obstruction cases hunger contractions were usually absent. Therefore, although it is agreed that in pyloric obstruction cases without atony gastro-enterostomy

results in lessened pressures on the ulcer area, yet in cases without obstruction this is by no means apparent. Certainly in Sick's case a midgastric fistula failed to relieve the pylorus from high pressure.

3. *That by being Placed at the Most Dependent Portion of the Stomach it Favors Gravity Drainage.* At operation we have repeatedly seen surgeons, imbued with this idea, strive to select the lowest point of the stomach; and, as Martin remarks, they even place the patient in upright posture after operation to favor drainage. The fact is that the lower border of the sto nach changes considerably during digestion, in the nearly empty stomach the pylorus becoming ordinarily the lowest or almost the lowest part. Moreover, as the stomach fills it rotates on an axis extending from the cardia to the pylorus. It can hardly be supposed then that what is the most dependent point at operation in a stomach rendered atonic by the anesthetic and in a patient lying on his back, will remain the most dependent point for any length of time during the digestive period after the stomach has regained its tone and the patient is upright.

As a matter of fact, however, in the ordinary alimentary tract food is not propelled by gravity but by differential pressures. Cannon and Blake showed in cats that after gastro-enterostomy, even though the animal was held up so that the opening was in the most dependent portion, water placed in the stomach did not run by gravity through the stoma into the jejunum but passed through only in response to the force of peristaltic waves. Therefore, in the ordinary case, gastro-enterostomy does not favor drainage by gravity. In the emptying of highly atonic stomachs in atonic abdomens with low intra-abdominal pressure, gravity may play a distinct role; yet in these cases unless there is pyloric stenosis the results of gastro-enterostomy are not highly encouraging.

4. *That it Favors Stomach Emptying Regardless of Gravity*, that is, by peristalsis. In regard to this I find a great discrepancy of opinion. In the roentgen-ray studies of Cannon and Blake on cats fed with fluid boiled starch the food passed regularly through the pylorus and not through the new stoma, with two exceptions, one where the stoma was in the vestibule close to the pylorus and the other where the stoma was large and in the anterior wall about half-way between the two ends of the stomach. Except for these two cases the pylorus was regularly the exit chosen, even though it was much narrowed by a ligature. This was in animals with no ulcer to cause hyperperistalsis and abnormality of pyloric closure. That both in man and laboratory animals the food mostly does pass the new opening to seek the natural outlet has been shown by others, *e. g.*, Tuffier, Delbet, Kelling, Guibe, Troell and Lewisohn; and Haertel, after the study of a large series of radiographs following gastro-enterostomy in man, observes that though in most cases food passes through both the pylorus and the new stoma, yet the peristaltic

wave is unchanged and continues to be directed as before toward the pylorus. Schueller, Petrén, Cole, Carroll and other radiographers have made similar observations.

On the other hand recent reports by C. H. Mayo, Carroll, Hartmann and Outland, Skinner and Clendenning point to the effectiveness of the gastro-enterostomy stoma; and Carman and Balfour, of the Mayo Clinic, emphatically state that the opaque meal regularly passes freely through the stoma even after years. Several observers have remarked, however, that while in the first few weeks after operation the food has taken its exit for the most part through the new outlet, yet later it has returned in large measure to the outlet through the pylorus. This might be explained by assuming that in the first few weeks the ulcer is still in the irritative stage and is effective in producing pyloric obstruction by pylorospasm; but that later, as the ulcer heals, it no longer excites pylorospasm, and therefore, as there is no longer obstruction, the food passes through the natural outlet. This would seem to be the desirable sequence of events. Truesdale showed that in some cases after the operation the pylorus, owing to disuse, undergoes atrophy and dilatation and remains permanently open. It is interesting to note how frequently in some of the relieved cases the roentgen-ray shows a six-hour residue. Smithies found an eight-hour food residue after a mixed meal in 16.4 per cent. of those returning for treatment. Carter notes an early emptying time when both pylorus and stoma are patent but delayed emptying when the pylorus is occluded at the operation. Wilensky and Crohn state that the emptying power of the stomach is not accelerated by gastro-enterostomy with pyloric blocking, but is actually retarded.

5. *That Whatever Good is Obtained is Due to the Diminution of Acidity* by the passage of bile and pancreatic juice into the stomach through the new stoma. It is Deaver's opinion that if a posterior gastro-enterostomy in ulcer of the pyloric region does any good at all it is by allowing bile and pancreatic juice to enter the stomach, thus producing a neutralizing effect on the acid contents. This is the opinion of many surgeons. It is true that following gastro-enterostomy the acidity tends to be reduced, for H. J. Paterson found that it falls on the average thirty points, and Smithies, in those returning for treatment after operation found a reduction in free acid and total acidity in about 80 per cent., the reduction averaging about twenty points, though in 17 per cent. there was no reduction and in 3 per cent. a rise in acidity. One month after operation Crohn and Wilensky found a slight average decrease in acidity though not a decrease in all cases.

The Effect of Bile and Pancreatic Juice on Acidity. Grey demonstrated by cholecystogastrostomy that when the total output of bile was made to pass through the stomach it did not materially affect the level of gastric acidity. He also deflected the total pan-

creatic juice into the stomach and likewise noted no material change in acidity. In a study of fractional curves after gastro-enterostomy Wilensky and Crohn observed that the influx of bile was frequently followed by a secondary rise in acidity and that at times the highest acidities were recorded when the bile was present in greatest abundance. These observations tally with our own experience and that of Smithies, that highly bilious stomach contents after gastro-enterostomy frequently show high acidities. H. S. Carter and Wilensky and Crohn have reported that a number of the operated cases gradually lowered their acidity until a complete achylia was developed. This could hardly have been due to a reflux of alkaline material. Therefore though acidities tend to be lower after gastro-enterostomy, they are not by any means always lower, and we do not believe that the diminished acidity is the effect of neutralization by regurgitated bile and pancreatic juice. As a matter of fact the degree of gastric acidity is unimportant in deciding the improvement after operation (Troell, Crohn).

To summarize our remarks on the desired effects of gastro-enterostomy we might say that *when there is obstruction* to the exit of food the operation permits stomach emptying and relieves the retention. But in *non-obstruction cases* it does not, at least to any great extent, relieve the ulcer-bearing region from peristaltic activity from the irritation of food and gastric juice and from high peristaltic pressures, it does not favor gravity drainage, it does not, as a rule, accelerate the emptying time, and it does not act through the neutralization of high acidity by the bile and pancreatic juice which it permits to enter the stomach. Therefore, except in cases of obstruction, due either to disease or to operative procedure, as in pyloric stenosis or pyloric removal and possibly hour-glass contraction, we are unable to discover a satisfactory reason for a good result from gastro-enterostomy. It would therefore seem a pertinent question to ask: Except in the presence of obstruction what useful function does gastro-enterostomy perform?

Gastro-enterostomy with Pyloric Blocking. On account of the numerous failures of gastro-enterostomy, and the frequency with which after gastro-enterostomy the food has passed in the normal direction through the pyloric exit even when this was partially obstructed, a number of surgeons have attempted to block the pylorus by means of a silk ligature. W. J. Mayo has concluded that such blocking gives no advantage, and this belief is concurred in by Scudder, Gonnerud and others; and as it has not been a successful procedure, it has largely been abandoned. But in its place has come pylorectomy or at least a severance of the duodenum from the pylorus. To this certain surgeons object, on the ground that it makes the operation a more severe one; that it makes a permanent obstruction no longer needed when the ulcer heals; that it favors high pressures in the ulcer-bearing region, and possibly that by

preventing the contact of hydrochloric acid with the duodenal mucous membrane, it prevents the formation of secretin, and hence results in a diminished secretion of pancreatic juice and bile. We do not think this last a factor, for three reasons, namely: (1) The absence of hydrochloric acid in cases of gastric achylia is not accompanied by a decrease in the secretion of bile and pancreatic juice; (2) hydrochloric acid can produce secretin in the jejunal mucous membrane, as shown by Bayliss and Starling; (3) in these cases there is obviously no lack of bile and pancreatic juice.

In several of our own cases, after a simple gastro-enterostomy had failed to relieve, a secondary operation was done to block the pylorus. We can recall two in which the ulcer had been well up on the lesser curvature and had been excised by the saddle incision, but pylorospasm persisted. They did well after the pyloric excision. We can recall three others in which the ulcer was at or near the pylorus, and the pylorus at operation seemed well stenosed, but the symptoms continued after the gastro-enterostomy. All did well after pyloric obliteration.

Normal Results of Gastro-enterostomy. A gastro-enterostomy regularly results in certain changes, namely: (1) The passage of the acid and sometimes highly acid gastric contents into a jejunum which is habituated only to material that is alkaline; (2) admixture of the gastric contents with the bile and pancreatic juice at an abnormally low point in the intestine; (3) the passage of some poorly disintegrated food into a jejunum accustomed to receiving material that is well chymified. After a mixed meal Smithies found with the stomach tube that the gastric contents showed poor chymification in only 10 per cent. of the cases; yet it would seem that, owing to the position of the stoma, some of the food must be forced through without chymification.

Untoward Sequelæ of Gastro-enterostomy. The most common untoward sequelæ are: Renewed ulcer symptoms, retention symptoms, nausea and fulness without retention, pain, and diarrhea.

Renewed Ulcer Symptoms after Gastro-enterostomy may result from: (1) Failure of the original ulcer to heal. After a remission of a few weeks or months brought about by the rest and diet following operation and similar to remissions after medical treatment the symptoms recur.

2. The development of a new gastric or duodenal ulcer.

3. The development of a true peptic ulcer in the jejunum below the stoma region.

4. The development of ulceration in or about the gastro-intestinal anastomosis. This is probably due in most instances either to trauma from the use of clamps as demonstrated by Troell, Coffey, White and Hamilton or to the employment of unabsorbable sutures. Pool, W. J. Mayo, Mann, Gonnerud, Woolsey and others have reported finding the linen or silk sutures projecting from the bases

of such ulcers. It may be due to careless feeding in the early post-operative period, for in a study of gastro-enterostomy in animals, Flint found the new-formed anastomosis to be the site of a healing ulcerated surface for about two weeks.

Retention symptoms may result from failure of the stoma or obstruction of the jejunum, because:

1. The opening is too far to the left.

2. The opening shrinks unduly. Finney had a case in which in spite of absolute pyloric stenosis the stoma had been reduced to the size of a straw. Von Eiselberg believes that reduction in size of the opening is almost always due to ulceration.

3. The opening is closed by distention of the stomach, which causes stretching of the jejunum over the stoma. Cannon and Blake noted in cats that when the stomach was distended by a large meal the food passed through the stoma with difficulty, so they excised a gastro-enterostomy stomach, tied its pylorus and filled it with water. As the gastric wall became stretched almost no water escaped through the stoma, the comparatively small jejunal wall having flattened out over the opening to become practically a part of the stomach wall.

4. The opening is closed by contraction against it of the cut circular fibers of the jejunum. In the words of Cannon and Blake: "The contraction of the cut circular muscles can have no other effect than to shorten and flatten the intestinal wall between the two lines of attachment." In two of our cases opened under local anesthesia vigorous peristaltic waves were present, and after the anastomosis had been made we observed that as each wave reached the cut in the jejunum the whole wall of the gut flattened against the opening, the effect of the contraction of the circular fibers that had been cut being just that described by Cannon and Blake. It was obvious that anything in the duodenum would shoot up into the stomach rather than pass into the distal limb of the jejunum.

5. The stoma or the jejunum is closed by volvulus or traction, as when the stomach recovers from its operation atony or when the patient reassumes the upright position.

6. The food fails to pass readily into the distal limb of the jejunum because of adhesions with kinking. The circular muscles proximal to this point being cut and stomach peristalsis being absent for many days following operation (Wilensky and Crohn), there is no driving peristaltic force to push the food along, break newly forming adhesions and straighten out a kink (Cannon). We have had two marked cases of obstruction by adhesions with pocketing of the jejunum at a distance of two or three inches beyond the stoma, the roentgen-ray showing immediate passage of food from the stomach, but partial obstruction at the lower point with pouching above.

7. The establishment of a vicious circle, the food that passes through the still open pylorus travelling back into the stomach

through the stoma. Cannon and Blake watched such a process for half an hour, during which time not an atom of food passed into the distal limb of the jejunum. They noted no untoward results from the vicious circle. Vicious circle is usually due to a plastering of the jejunal wall against the opening or to obstruction of the distal limb of the jejunum. Probably it is a cause of untoward symptoms less frequently than usually supposed.

Nausea and Fulness without Retention may result from: (1) Too rapid emptying of the stomach. In feeding with the duodenal tube it has been found that passage of the food too rapidly or at a temperature much above or below that of the body is prone to result in feelings of distention, nausea, weakness or even collapse, symptoms quite the same as in occasional cases after gastro-enterostomy. (2) Possibly though not certainly from too abundant regurgitation of bile. In practically all cases after gastro-enterostomy bile is regurgitated into the stomach yet no nausea ensues. But in two striking cases during the periods of nausea we have noted excessive quantities of bile in the stomach contents, while in the same patients when free from nausea there was very little bile. We have been inclined to attribute the nausea to the abundant bile in the stomach though it is possible that the responsible factor may have been something else, the extra bile having regurgitated as the result of gagging. For though bile when swallowed is nauseating, yet fresh ox-bile has been administered by stomach tube by John Gerster without nausea.

Pain is usually the result of ulcer or adhesions, especially adhesions to the anterior abdominal wall.

Diarrhea is probably a sequel either to a too rapid emptying of the stomach, to irritation of the jejunum by either the acid stomach contents or coarse food particles, to changes in the pancreatic secretion, or to a superabundance of fat in the food (Cameron).

From Matthieu's Clinic at the St. Antoine, Paris, it was reported that very few if any of their cases of gastro-enterostomy, if followed over a sufficiently long time, failed to show some pathologic symptoms, gastric or intestinal.

In a study of cases following posterior gastrojejunostomy with exclusion or removal of the pylorus, Wilensky and Crohn found that 11 did well after the operation, though it was necessary to curtail the amount of food permitted, 14 showed definite disturbances in physiology and 7 showed mechanical disturbances in the functions of the gastrojejunal stoma. In almost all there was absence of peristalsis one month after operation.

In the group that apparently did well motility and acidity were slightly diminished and there was a distinct and persistent hypersecretion.

In the group with physiologic disturbances there were mental depression with poor nutrition, pain, vomiting, occasionally hema-

temesis, and constipation or rarely diarrhea. There were definite delay in motility, hypersecretion with a high acidity curve to the end of digestion and a poorly functioning stoma, produced not by stomal closure but by disturbed muscular function.

In the group with mechanical or organic changes at the stoma there were markedly delayed motility with retention, a high acidity curve, violent peristalsis, six-hour roentgen ray residue and insufficient or closed stoma.

Summary. Considering all the possibilities we have mentioned and other postoperative complications, such as hernia, rectus diastasis, gastro-intestinal fistula and various unmentioned abdominal adhesions, and in addition the operative mortality and the number of cases that after a period of relief show relapse similar to that following medical relief, we must feel that surgery in an ulcer case must not be too lightly resorted to. As Wilensky and Crohn say, "It is evident that the impression that gastrojejunostomy is an operation which in no way impairs the functional efficiency of the stomach is an erroneous one. In only a minority of the cases does the stomach return to an almost normal state of functional activity."

We do not wish, however, to disparage the use of the operation in the proper case, and would say with Crohn that we could not treat disorders of the stomach without using gastro-enterostomy. But its value is to make an exit for food when the normal exit is not available. And we hold with Torek that "the treatment of ulcer of the stomach is essentially medical and not surgical, and that it is only certain of its complications or sequelæ that require surgical intervention." We now leave the subject of gastro-enterostomy.

Cases of Ulcer which Require Operation. The emergency cases we have already considered. Of the others we have those in which surgery is imperative from the outset and those in which surgery should be resorted to only after thorough medical treatment.

Surgery Imperative. We consider surgery imperative and medical treatment futile in the following conditions, namely: (1) Chronic penetration as shown by radiographs; (2) palpable induration; (3) adhesions which cause distortion of the stomach, interference with peristalsis or much pain during the digestive period; (4) permanent hour-glass; (5) pyloric stenosis not syphilitic; (6) repeated copious hemorrhages; (7) conditions which suggest that an ulcer is becoming carcinomatous. In duodenal ulcer, as carcinomatous change rarely occurs, this is not of moment; but since in gastric ulcer this change is not infrequent, its possibility must induce an earlier consideration of surgery.

Surgery only after Expert Medical Treatment. The majority of peptic ulcer cases can, in our opinion, be definitely said to require surgery only after the failure of thorough and prolonged medical treatment. When a case is medical the relief of symptoms (not the

cure) by treatment is, as a rule, quite prompt. Therefore, on the one hand, the failure of the treatment to relieve the symptoms suggests that the case is probably surgical; whereas, on the other hand, when a case seems in all likelihood surgical, but not certainly so, a course of medical treatment is advisable to prove the point. Furthermore, if the patient shows a positive Wassermann reaction or gives a history or any physical evidence of syphilis, antileutic treatment should be tried.

Given a thorough medical trial by someone competent to supervise the treatment, we should consider those cases surgical which continue to show: (1) Persistent or recurrent hemorrhage even small in amount; (2) pain; (3) nausea; (4) pylorospasm of such persistence as to simulate pyloric stenosis; (5) inability to ingest comfortably the ordinary wholesome foods permitted by the circumstances of the patient, this making the poor patient a surgical case earlier than the well-to-do one; (6) inability to ingest comfortably enough food to maintain nutrition while living a normally occupied life; (7) recurrence after apparently a cure. Or, as C. H. Mayo expresses it: "The best type of gastric case for surgery is that in which every method of medical treatment has failed or the patients have become tired of the rigid diet and care which are necessary to relieve or to prevent relapse." This is our answer to the question when to operate in peptic ulcer cases. We shall not attempt to answer the question when to perform a second or a third operation if symptoms persist.

When an ulcer case is referred to the surgeon the physician must still feel his responsibility to the patient, and in order to provide against having a surgical failure follow the medical failure should urge the serious attention of the surgeon to the following statements, namely: that of Ginsburg, that "small quantities of food at frequent intervals have a better physiologic effect upon the recently short-circuited stomach than three daily meals;" that of Cannon, that "after gastro-enterostomy, effective action of the anastomosis demands that there shall not be more than a moderate distention of the stomach;" and that of Troell, that "the recurrence of symptoms following operation in many cases depends to a considerable degree on the surgeon's neglecting to give dietetic and other prescriptions suitable for ulcer." We would commend the counsel of W. J. Mayo that "following surgical intervention the patient should be under good medical advice until permanent cure is assured;" and that of Carter that "after operation every opportunity for healing and cicatrization should be given, involving, as this does, weeks or months, during all of which time the diet should be bland, soft and free from thermal, mechanical or chemical irritants." No longer should we tolerate a surgeon who places an ulcer case on heavy and bulky diet within two or three weeks of his operation.

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THE PRINIPLES UNDERLYING THE SAFE AND MORE RAPID EVOLUTION OF THORACIC SURGERY[1]

By Willy Meyer, M.D.,
NEW YORK.

Mr. President, Ladies and Gentlemen:

While a dozen years ordinarily may represent an age in our times, they mean hardly more than a few months in medical science; and so, I hope, you will understand when I frankly state that, though I have all of eleven years to my credit in active clinical work as well as in the study of the literature on the subject, I consider myself no more than a mere tyro in thoracic surgery.

It took abdominal surgery fully forty years to develop to its splendid status, no small part of which was accomplished right here in Rochester. Nevertheless, every day, one might say, sees the great edifice of our abdominal work enlarged by some addition. It is true that thoracic surgery had the benefit of all the experiences gained in abdominal surgery as well as the additional asset of having started with a most perfect asepsis. But in spite of all this I hardly think we shall go much amiss in predicting that there will still remain problems to solve for our children and children's children.

Attention should be called briefly to the principal practical differences between abdominal and thoracic surgery. When we make an incision to reach a diseased organ within the abdominal cavity, *e. g.*, stomach, liver, appendix or what else it may be, if the anesthetist is efficient, the asepsis faultless, and we know how to do the required work, the majority of our patients recover. In the interval operation for appendicitis, for instance, we see of 100 patients 100 get well. When we cut into the abdomen, having divided the wall of this cavity and also the outer layer of the sac, which we call peritoneum, its contents lie before us in their anatomical relation as well as remain undisturbed until we disturb them; the respiration and the circulation of the blood, too, continue without disturbance. With perfect ease and equanimity we can go about our task. But in thoracic surgery the matter is not quite so simple. Granted the same perfection in every technical detail as before, every time a thorax is opened "something" happens that does not happen when the abdominal cavity is opened. It announces itself by a hissing sound. What is this something?

When we make an incision between two ribs, carefully separating layer after layer of muscular tissue, and at last also dividing the septum which we call the pleura, we open thereby the pleural sac

[1] Read before the Southern Minnesota Medical Association, Rochester, Minn., June 23, 1919.

which protects the lung. Under normal conditions the lung completely fills the space between mediastinum and chest wall, and the pleural sac surrounding it contains neither air nor fluid, excepting only a small amount of viscid, glue-like substance that permits the leaves of the pleura, the one covering the wall of the chest, mediastinum and diaphragm, the other covering the lung, to glide upon one another without perceptible friction, as two panes of glass do when there is a film of water between them. We have, then, under physiological conditions no air on the outside of the lung, but on the inside of the lung we find the pressure of the atmosphere, and this pressure keeps the elastic fibers, of which the lung tissue is largely built up, distended. This condition is changed through our incision which, being made for operative purposes, is usually a large one. The air has now free access to the space from which nature had it carefully excluded, and it is then that this "something" happens to which I have previously alluded: the large, freely expanding and contracting organ, the lung, that we had met upon opening the chest, suddenly leaves the inner chest wall, loses its contact with it and before our eyes becomes smaller and smaller until, no larger than a man's fist, it comes to rest near the spinal column. It has been put out of commission. The collapsed lobes no longer take part in the function of the lung of ventilating the blood, feeding it with oxygen and freeing it of the excess of carbon dioxide, and the space previously filled with the lung has become a large, empty cavity. Why does all this happen? It is due to the equalizing of air-pressure upon the inside and upon the outside of the lung. The one-sided air-pressure upon the inside only, which, as explained, kept the elastic fibers distended, being now counteracted by the equally great air-pressure admitted through our incision to the outside of the lung, leaves the contractile strength of the elastic fibers as the only active force present, and, unless the lung should happen to be adherent to the chest wall, it contracts down upon its pedicle, the bronchial tube, which enters it near the bifurcation of the trachea.

But that is not all. This is only what immediately follows the hissing noise of which I told you before. Something else happens. The thoracic cavity is divided in the center by a structure reaching from spine to sternum, which we call the mediastinum, with lung to the right and to the left of it, and in which are located the heart, the large bloodvessels connecting heart and lung, nerves and other soft tissues. From mere enumeration of these parts as the very seat of life itself, you will understand the importance of their being left undisturbed in their various functions. That, however, is just what is not the case after one side of the lung has collapsed. The patient makes strenuous efforts at breathing with the closed side of the lung and thereby sets the mediastinum in motion to the right and to the left, like a sail flops in a head-on breeze, which, like the mediastinum,

is fixed above and below. This to-and-fro motion of the mediastinum interferes with the proper ventilation of the still functionating part of the lung, and thus, though only one side is opened to the outer air, nevertheless both sides of the lung are injuriously affected. All this occurs only if the tissues within the chest are in their virgin condition. If in consequence of inflammation or other causes the soft mediastinal structures have become harder and more resistant it does not take place.

The condition just described is called pneumothorax, from the Greek "pneuma"=air, the term meaning: air in the thorax; it is unilateral or bilateral, according as to whether the outer air has direct access to one or both sides of the lung. The bilateral pneumothorax, unless promptly corrected, is always fatal; the unilateral is not always that. It seems that about 40 to 50 per cent. of patients are able to stand a unilateral pneumothorax; but, unfortunately, we have no means of knowing beforehand whom we may include in and whom we must exclude from this percentage. It is the same as in appendicitis, where the great majority of patients who have had one attack will have another sooner or later of which they may die. We cannot possibly know beforehand who will and who will not have a recurrence, therefore the rule that the inflamed appendix must be removed in every case, either during or soon after the first attack. It is a wise precaution. Along the same line of reasoning, if we know of a method to forestall pneumothorax, unilateral or bilateral, should we not apply it, thereby increasing the patient's chances of recovery? Surely, and more than that, it is our duty to do so. This method exists. This method consists in the use of apparatus designed to prevent the described effects of the inrush of air into the pleural cavity upon incision for operative purposes, and the general conditions here outlined as prevailing during the operation constitute the first principal difference between thoracic and abdominal surgery.

We now turn to the second principal difference between these two branches of surgery and find the same to pertain to conditions after the operation—to the after-treatment. Peritoneum as well as pleura tend to form adhesions after the operative wound has been closed, but the pleura has an additional tendency which the peritoneum has not equally outspoken. The pleura, being more sensitive to traumatism, discharges into the pleural cavity a fluid which we call an "exudate." Despite the most rigid asepsis this exudate does not always remain sterile, nor is it always absorbed. It may require drainage later on and may give rise to serious complications. A casual observer may here say: "Why not drain from the corner of the wound when closing up," or "Why not close the wound completely and drain through a lateral stab?" One thus arguing overlooks the air that would filter in alongside the tube, producing an "acute postoperative pneumothorax," which is no less

dangerous and often has the same fatal consequences as the above described acute operative pneumothorax.

Again I ask, would it not be a great step in advance if the danger of the postoperative pneumothorax could also be forestalled? If we could close up the thorax air-tight after the operation and yet drain? And this is the second point I want to bring out: We are able to do this. A method of air-tight drainage has been evolved which is safe and reliable and eliminates, barring an unforeseen accident, the danger of the occurrence of a postoperative pneumothorax.

I should be happy had I succeeded in holding your attention until now, but in the balance of my address I shall have to become more technical and address myself more to the medical men who good-naturedly have permitted me to explain to the ladies what to them is a matter of general knowledge.

I propose now to take up and discuss the two points before developed, *viz.*, the prevention of the acute pneumothorax (collapse of the lung), during the operation and the prevention of the acute pneumothorax during drainage after the operation.

1. **Avoidance of the Acute Operative Pneumothorax.** The construction and use of apparatus for thoracic operations began in the middle of the 90's of the last century, when Quénu, of Paris, worked out an apparatus on the lines of a diver's helmet, in which the patient's head was placed under increased air-pressure together with a sponge saturated with chloroform. Tuffier, of Paris, soon after advocated and practised the use of insufflation of air into the trachea. They tested their suggestions by animal experiments which one of them, at least, followed up with thoracic operations on the human subject in the hospitals of Paris, avoiding the effects of an acute pneumothorax.

America, above all, has a right to be proud of the pioneer work she has rendered in this field. I am referring to the valve apparatus for artificial respiration worked out by Fell and to the pump apparatus constructed by Matas, of New Orleans, both designed on the basis of the O'Dwyer tube. In 1898, Parham, of New Orleans, made use of Matas's apparatus in a resection of the chest wall for tumor, the first recorded thoracic operation under differential pressure in this country. His patient recovered.

However, this case and similar ones remained isolated. They were interesting cases, and there it ended. More concerted action resulted when the differential pressure idea was conceived anew by F. Sauerbruch in 1903. He had been charged by his chief, the late Prof. v. Mickulicz, of Breslau, to find a method which would make work in the thorax as safe as that in other cavities of the body. The construction of Sauerbruch's negative chamber in the following year was the result of this work. Thus the year 1904 marks the real beginning of thoracic surgery by the transpleural route. The

apparatus designed for experimental work consisted of a box with the animal's head outside and the chest and body inside. A cut-out with rubber collar in one of the sides of the rectangular box served for the passage of the neck of the animal, surgeon and assistant sitting inside the box. The air-pressure in the box was reduced by machinery to a degree equalizing the force of the physiological force of contraction of the normal elastic lung tissue. This having been done, transpleural incisions could be made in the intercostal spaces right and left, or large flaps of the chest wall be raised, the animal continuing meanwhile to breathe as if nothing had happened. Upon reversing conditions the animal's head being put into the box and the body outside and the air-pressure within the box being increased, the same phenomenon, *i. e.*, non-collapse of the lung, was observed when the thorax was opened and the animal breathed the increased pressure.

On the basis of the artificial reduction of the air-pressure within the chamber below the normal atmospheric pressure, considering the latter as zero-pressure, this operative procedure was called "operation under negative pressure." The method as such was termed "operating under difference in air-pressure," or, briefly, "under differential pressure." In 1904 a large chamber, made of iron and glass, for operations on man was in use at Breslau.

Four years later an amplified type, constructed on the basis of Sauerbruch's principles, was built in New York and is now a part of the instrumentarium of the Thoracic Pavilion of the Lenox Hill Hospital of New York City. It is the only one in America.

The negative chamber represents an enlarged pleural cavity and is the most "physiological" apparatus in existence for complicated intrathoracic work upon weak and reduced patients. It permits of the use of differential pressure under general as well as local anesthesia. It is a splendid physical apparatus and will forever retain its scientific as well as its practical value. But the negative chamber is expensive and stationary, surgeon, assistants, nurses and patient have to go to the apparatus; the apparatus cannot be brought to the patient.

For this and other reasons the attention of the surgical world turned more to the positive differential pressure method, as first represented by the positive cabinet and its modifications. In quick succession three additional, useful procedures of employing positive air-pressure have been perfected: The mask method (1908); intratracheal insufflation (1910) and pharyngeal insufflation (1913). In each of them the lung is blown up artificially in order to overcome the pressure upon the outside of the lung of the atmospheric air, which communicates with the interior of the pleural sac by way of the incision.

The employment of any one of the four methods mentioned enables us to avoid the collapse of the lung on incising the pleural

cavity when adhesions between lung surface and chest wall are not present. In other words, any one of these four methods enables us to avoid the occurrence of the acute pneumothorax with its sequelæ and, therefore, makes work in the thorax perfectly safe.

In 1914 the opposition originally aroused by the differential pressure method as employed in thoracic operations had almost ceased. The method was recognized as safe for operative work within the chest by the great majority of colleagues interested in this branch of work.

In 1914 the war broke out and with it came a recrudescence of opposition.

Personally, I am fond of opposition, because opposition stimulates discussion and discussion is the foundation of progress. It was principally for the purpose of free discussion that the "American Association for Thoracic Surgery" was founded three years ago. But opposition must be constructive and not destructive. In this particular instance the opposition, to my mind, is decidedly destructive.

When the war came many of the men who went overseas were suddenly confronted with important traumatic chest cases and were compelled to do chest surgery without previous practical experience in this line. After temporizing for a time, they became aggressive, opened the injured chest widely, did the required work as in other parts of the body, closing the thorax as they were accustomed to closing the abdomen and saw splendid results, though no differential pressure apparatus had been used. No wonder they became enthusiastic and soon proclaimed: "There is no fundamental difference between operation within the abdominal and thoracic cavities; differential pressure is an unnecessary ballast; we can well get along without it." And, in order to carry his point, one renowned colleague even suggests the division of thoracic surgery into different chapters, requiring different types of operation, *e. g.*, lung surgery and esophageal surgery.

How can we explain the discrepancy between the experience in thoracic operations at or near the front and as seen in peace practice at home?

It has been stated on the basis of investigations made during the war that 50 per cent. or more of the patients with penetrating chest wounds died on the battle field. Those who reached a hospital behind the lines were the ones who had not succumbed to the effect of the acute pneumothorax and hemothorax, *viz.*, the sudden entrance of air plus blood into the chest. Let us remember, further, that these soldiers were young men in the prime of life, who had not been sick for months and years, as is the case with the majority of patients whom we are called upon to treat for thoracic disease in times of peace. On these young and strong men, who had survived all the immediate consequences of the injury of the chest, our colleagues

who were abroad were called upon to operate; on these they gathered their experience. Under aseptic precautions they made an incision of the required length—and the long chest wound usually is better for the wounded than a small one, which latter often permits air to enter the chest, but not to leave it readily—pulled the lung forward and held it in front of the wound for the necessary work. The mediastinum now could not flop from one side to the other, the well-known method to avoid the development of the symptoms of the acute pneumothorax (Müller's trick). The mediastinum is thus steadied during the operation and the lung is attended to as the case may require and then dropped back. If the chest was closed air-tight the great majority of patients had a good chance of recovery and were seen to recover.

With this impression in mind, renowned medical men have come from England, France and Italy in the course of the last three years to visit us. They have travelled through our country and have given us the results of their personal experiences. Some of them had been carried away by the favorable results obtained in traumatic chest surgery, done without any apparatus, on soldiers who had survived the shock and the effect of acute pneumo- and hemothorax, done while the soldiers were still suffering from them, and they wondered why any surgeon had ever thought it necessary to make special provision for an interference in the interior of the chest.

I have the greatest admiration for their medical courage, to take up under such adverse circumstances a new line of operative work and, what is more, make a success of it. All honor to them!

On the other hand, I cannot help asking is it right to draw such sweeping conclusions from the experience in one small part of the surgery of the chest—the traumatic—with reference to thoracic surgery in its entirety? To my mind it is not permissible.

To show how discussion helps in clearing up a fundamental question like the one we are considering allow me to cite a personal experience: When the commission of surgeons from the front, consisting of three representatives from England, one from France and one from Italy, came to attend the American Congress of Surgeons in October, 1918, they visited the Lenox Hill Hospital of New York City and looked over the thoracic apparatus there installed. After a heart-to-heart talk of almost two hours on the means at hand today, to avoid or overcome the acute pneumothorax in chest operations, three of the five gentlemen joined me in the stand: that we do need the differential pressure method for safe operating within the thorax.

I most fervently hope that those colleagues who still think differently, because they have had favorable experiences in chest surgery without the employment of apparatus, will come forward and relate their observations. If their charts prove that the work can be done equally well and equally safely for the patient, without

apparatus, why should we trouble ourselves with differential pressure methods? why should we not throw all apparatus overboard and proceed as in other parts of the body? I for one still believe that if we had one hundred patients with surgical chest disease and gave fifty cases each to two surgeons who commanded equally good technic and perfect asepsis, one working with apparatus and maintaining the physiological working of the lung during the operation, the other one working without apparatus, I say, I feel sure, that the one who used the differential pressure method would get a higher percentage of recoveries than the one who did not use it.

2. **Avoidance of the Acute Postoperative Pneumothorax and of the Accumulation of the Pleural Exudate by Means of Air-Tight Thoracic Drainage.** In my endeavors to drain the chest and, incidentally, to avoid the occurrence of the acute postoperative pneumothorax I have at last decided upon a method of choice. It is an adaptation to general operative work of the method of air-tight drainage used by Dr. Kenyon, of New York City, in the treatment of empyema in children, and practised in a similar way, for the treatment of the same disease in patients of any age, by Buelau, more than twenty-five years ago. I consider it a universally useful method for draining the chest air-tight, after any and every kind of intrathoracic work. To keep the patient with free (not air-tight), thoracic drainage under the influence of differential pressure within the apparatus, negative chamber or positive cabinet, as worked out at our hospital six or seven years ago, is also an excellent method, but it is cumbersome.

Of another evidently useful method, Tiegel's metal drain, with valve arrangement at its outer end, I have no personal experience.

Today, before closing the chest incision completely by layer sutures, we make a stab one or two interspaces lower in the posterior axillary line, introduce in air-tight fashion a rubber tube about as large as the third finger of a man, the tube having one or more side holes near its inner end and outside a short glass tube interposed, fasten it securely with broad adhesive plaster strips and let its free end dip into a graduated siphon bottle, which is partially filled with sterile water or some kind of antiseptic solution. Our observations and results have shown this to be a splendid and reliable method for accomplishing our purposes. One can see in the glass tube the quality of the secretion and measure in the siphon the quantity discharged within a given period. At the same time this method thoroughly and safely fulfils the demand made by those most experienced in thoracic surgery: to always close the chest air-tight in order to allow the lung to expand at once.

The two principles underlying the safe and more rapid evolution of thoracic surgery, as I see them, then, are:

1. The use of the differential pressure method in order to avoid the occurrence of an acute pneumothorax during operation.

2. The immediate and complete closure of the incision in conjunction with air-tight thoracic drainage after every case of thoracic operation in order to avoid the acute postoperative pneumothorax as well as the accumulation of exuding fluid within the pleural sac.

(A series of lantern slides then illustrated the points previously discussed.)

SURGICAL TREATMENT OF PLEURISY.*

By J. L. Yates, M.D.,
MILWAUKEE, WIS.

Progress in the operative treatment of pleuritic effusions has until recently, been impeded by the concentration of surgical attention upon the curative therapy of empyema. This is an important part of the problem, but only a part, as purulent pleurisy is merely the late stage of some of these affections. The first therapeutic advance, made about five centuries B.C., was the conversion of a closed into an open pyothorax to start drainage. The second notable step forward, taken some twenty-four centuries later, was the conversion of an open pyothorax into a closed thorax to stop drainage. A third line of progress, starting with this latter period, has developed a method of air-tight drainage whereby both prophylactic and curative measures can find their simplest application.

Open thoracic drainage was introduced by Hippocrates, who recognized that simple acute, fetid or chronic empyema could be idiopathic, traumatic, postpneumonic or precede or follow phthisis. He learned that the drain should be placed low and that open drainage should neither be established too early nor be permitted to proceed too rapidly. Twenty-four hundred years' experience and observation have added very little to these teachings.

Closure of an open pyothorax has always been a serious problem because a proportion of individuals fail to heal spontaneously after thoracostomy. No doubt Hippocrates was confronted with the identical dilemma of a death from amyloid disease, an operative failure or considerable physical and functional disability. There are but three ways healing can be fostered under these conditions: (1) By collapsing the thoracic parietes against the retracted lung through some form of costoplasty, a method with which the names of Estlander and Schede are associated; (2) by releasing the adhesions surrounding the collapsed lung, the principle of decortication of Delorme and thereafter expanding the lung to meet the parietes; (3) by obliterating the intrapleural space with tissue transplants or

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by the introduction of some form of synthetic filling compound into this cavity in an attempt to obtain ultimate repair. Each of these methods implies a means of securing adequate tissue disinfection, *e. g.*, excision, lavage, chemical action.

H. I. Bowditch,[1] of Boston, began in 1850 to aspirate and to reaspirate in the treatment of pleuritic effusions. He proved that such treatment was efficacious in combating pleurisy as well as in preventing and in curing empyema. This celebrated internist must be given great credit for having demonstrated the wisdom of treating pleurisy by early air-tight, one-way drainage.

The foregoing summary includes the methods essential in treating pleurisy if applied so as to coöperate with natural defensive reactions. Pleural resistance is highest when pleural surfaces are in apposition.[2] Such apposition can be maintained or reëstablished only when there is adequate pulmonary inflation. Pleuritic effusions are produced more rapidly than they are absorbed, and if they are not removed pulmonary deflation and pleural separation are inevitable. Drainage is therefore positively indicated in the early treatment of pleurisy, and it must be air-tight, one-way drainage or pulmonary deflation and pleural separation are again assured.

There is now available an abundance of evidence exemplified in the reports of Whittemore[3] and McKenna[4] to prove that results obtainable by this method of drainage treatment are superior to any yet recorded when the immediate mortality and the duration of convalescence are considered. In addition there is a more nearly perfect restitution of health through the preservation of the tripod upon which functional integrity of respiration depends, namely, free mobility of the thoracic parietes, normal intrapleural negative pressure and unimpaired pulmonary elasticity.

Air-tight, one-way drainage, whether employed interruptedly by aspiration or constantly as a catheter drain inserted through a rib or between ribs, or as a rigid tube sewed into a defect produced by rib resection, has been proved efficacious in controlling traumatic pleurisy, including the type following thoracotomy,[5] in reducing the irritations of acute simple pleurisy and in promoting recovery from empyema either with and without lavage. To this list I can add the control of encapsulated (interlobar) empyema and of tuberculous and carcinomatous pleuritic effusions.

This simple drainage is, however, not a panacea. It will reduce the number of major operations and minimize the severity of those which cannot be avoided, provided it is properly used. The method advocated consists in intercostal insertions by means of a trocar

[1] Boston Med. and Surg. Jour., 1884, cxl, 572.
[2] Yates, J. L.: Annals of Surgery, 1920, lxxi, 241.
[3] Boston Med. and Surg. Jour., 1919, clxxxi, 575.
[4] Bulletin of Chicago Medical Society, 1920, xix, 22.
[5] Laboratory of Surgical Research, A. E. F., Boston Med. and Surg. Jour., 1919, clxxx, 405.

of one or more 16 F. catheters, provided with check valves, at the most favorable level for drainage (and lavage) compatible with the patient's comfort, which is determined by possible limits of activity, by whether the individual be bedridden in one position or is able to sit up or even to walk. The force required to expel the exudate, reëstablish normal negative pressure and pulmonary inflation is furnished by the increased intrathoracic pressure of deep inspiration. No strong suction is required though a constant slight negative pressure is often essential to prevent the serous exudate from coagulating within the drainage tube. The tip of the catheter should be introduced far enough to function but not far enough to make avoidable contact with the expanding lung. Such an introduction can be made accurately only with fluoroscopic control. The insertion is done under local anesthesia after so dislocating the skin that when the catheter is withdrawn, the skin in resuming its normal position acts like a check valve in closing the drain track. If drainage be required for more than a week the tubes must be then removed and reinserted at another point or there will be danger of air leakage around the tube, a danger which becomes a certainty a few days later.

If the tubes are improperly inserted through the skin, at the wrong level or to too great extent and allowed to remain overlong in one position, all of the conceivable misfortunes connected with the most disastrous complications of both closed and open pyothorax can develop. In addition the insertion of a trocar uncontrolled by a fluoroscope can wound the diaphragm, the lung or even the pericardium. Irrigations, if attempted too early, can disseminate infection or break down limiting adhesions. If given too forcefully they can cause similar catastrophes or lead to dangerously violent paroxysms of coughing or choking, particularly when the first lavage is not done with salt solution and Dakin's solution is too irritating. This is certain to be the case if a bronchial fistula is present.

The invaluable lessons come from failures. The blunders above enumerated have been observed. In a group of empyema patients treated improperly by simple drainage the mortality rate and the proportion of serious complications, especially open pyothorax with a firmly contracted lung, were much higher than they would have been had routine Hippocratic open drainage been employed. It is fair to assert that if principles are given proper attention methods will take care of themselves. This is true providing the gross folly of being principle-wise and procedure-foolish is avoided.

Quoting from Bowditch: "It (aspiration) has been of infinite service to mankind and will ever continue to be such. It will save lives which without it will be lost. All that is required is that due care govern the use of it."

CAN THE GALL-BLADDER, BILIARY DUCTS AND LIVER BE MEDICALLY DRAINED?

A FURTHER CONSIDERATION OF SOME ASPECTS OF DIAGNOSIS AND TREATMENT OF CHOLECYSTITIS AND CHOLEDOCHITIS BY A METHOD OF PHYSIOLOGIC DRAINAGE. THIS IS THE FIFTH OF A SERIES OF PAPERS ON THE GALL-BLADDER.[1]

By B. B. Vincent Lyon, M.D.,

ASSOCIATE IN MEDICINE, JEFFERSON MEDICAL SCHOOL; CHIEF OF CLINIC, GASTRO-INTESTINAL DEPARTMENT, JEFFERSON HOSPITAL, PHILADELPHIA; VISITING PHYSICIAN, METHODIST EPISCOPAL HOSPITAL.

In a previous paper[2] I called attention to a direct, non-surgical method of draining the biliary apparatus. In that paper I mentioned the fact that the experimental observations on dogs by Meltzer[3] aroused my curiosity and created the desire to extend those experimental studies to human beings.

As a prelude to your understanding the principles underlying this method of non-surgical drainage, you must known that Meltzer found that when he directly douched the duodenum with a solution of magnesium sulphate he could cause "a completely local relaxation of the intestinal wall," and that this relaxing effect was not observed when this salt was administered by mouth and allowed to pass across the gastric mucosa before it reached the duodenum. Meltzer then suggested testing, by means of the duodenal tube, in jaundice and in biliary colic, the local application of a 25 per cent. solution of magnesium sulphate. "It may," he says, "relax the sphincter of the common duct and permit the ejection of bile, and, perhaps, even permit the removal of a calculus of moderate size wedged in the duct in front of the papilla of Vater."

This very interesting observation of Meltzer's, although mentioned in an inconspicuous footnote, seemed to be pregnant with much practical importance. His paper was published in April, 1917, and that same month I began my first clinical experimental observations on human beings by means of the duodenal tube and various solutions of epsom salts and other substances. During the past thirty-two months I have made over 1200 biliary taps on 121 different patients,[4] both for diagnosis and treatment, and I have

[1] Read before the Section of Practice of Medicine, College of Physicians, Philadelphia, Pa., January 26, 1920, and Academy of Medicine, Cincinnati, Ohio, February 2, 1920.

[2] Reprinted from the Journal of the American Medical Association, September 27, 1919, lxxiii, 980-982.

[3] Am. Jour. Med. Sc., April, 1917, cliii, 469.

[4] Since the presentation of this paper in January, 1920, to date of publication, the total number of cases studied by this method has reached 309, with a total number of biliary drainages of 2240.

become more and more convinced of the practical ease with which both the normal and the pathologic biliary apparatus can be drained of its contents, with certain exceptions and within certain limitations, to which I shall refer later on. Further than this, I believe it possible to segregate and study bile obtained from the duodenum, from the bile ducts, from the gall-bladder and from the liver. I do not mean you to infer that this segregation of bile can be made so sharply that it can be said positively that any given sample is derived *exclusively* from the bile ducts or from the gall-bladder or from the liver, but segregated to the extent that it is possible to infer that the *larger amount* of the various types of bile recovered during a biliary tap is being drained from the ducts, from the gall-bladder or from the liver. If this much is admissible I believe it possible by cytologic, cultural and chemical studies of these various portions of segregated bile to make certain inferential diagnostic deductions as to the condition of health—physiologic or otherwise—or disease within those ducts, that gall-bladder or that liver.

In my first paper I attempted briefly to classify the types of bile thus segregated from cases of choledochitis, cholangitis, cholecystitis and cholelithiasis on the basis of their cytology, bacteriology, chemistry and their gross appearance. The interest with which that paper has been received in various parts of the world has encouraged me to present further observations of diagnosis and treatment by this method and to include a few case reports.

In presenting these observations I shall endeavor to record the phenomena which I have seen, to try to separate facts from theories and to hope to correctly interpret these facts and to substantiate these theories. Although I admit that personally I have arrived at certain very attractive conclusions from my studies I shall endeavor to refrain from stating them, because I realize that conclusions, especially if premature, often take on the undesirable characteristics of the boomerang.

For a clear understanding of what will follow in this paper it will be necessary to briefly allude to the anatomy, histology and physiology of the biliary system, which consists of the liver, the gall-bladder and the bile ducts. For the purposes of this paper I can describe the anatomy of the biliary system in a somewhat primer-book fashion as follows: The liver, the largest of the digestive glands of the body, is an organ whose substance is made up of myriads of bile-secreting polyhedral cells and certain stellate cells (Kupffer) arranged in the form of a lobule. Each lobule is supplied with blood coming from the portal vein and from the hepatic artery. In the portal vein the blood carries soluble substances absorbed from the intestines, certain of them useful substances, such as the various glucoses and proteids, which are reabsorbed by the liver for further use, and certain waste products drained from the organs emptying into the portal vein and which the liver must excrete. The hepatic artery brings to the liver cells themselves their daily

pabulum, which permits them to carry on their function of absorption and secretion. Each lobule, too, is furnished with a rather complicated network of vascular and bile capillaries, but for my purpose it is enough to recall the fact that the bile capillaries run in minute grooves or canals between the trabecular-like tubules of liver cells, which they drain and empty the bile into the interlobular bile ducts. These interlobular ducts are collected in larger channels, which in turn carry the bile into the right and left hepatic ducts and thence out of the liver. The lymphatics and nerves to the liver follow somewhat the same general arrangement. The liver, therefore, has three principal functions: absorption, secretion, and excretion. It absorbs from the portal blood soluble products from the intestinal tract—notably sugar, proteid, bile salts and pigment—which are acted upon by the metabolism of the liver cells before being stored up in the liver or passed back again into the general (blood or bile) circulation. It secretes a fluid substance called bile, which is of great aid to proper digestion, particularly acting as a co-partner with the pancreas in the absorption and digestion of fats. By means of the bile it excretes waste products and bacteria brought to it by the portal blood and probably by means of metabolic activity of the liver cells filters out, or neutralizes, toxins, both chemical and bacterial. The bile is carried from the liver by the right and left hepatic ducts, which soon unite into a larger one, and are joined by the cystic duct, and their union forms a larger (or common bile) duct, which empties the bile into the very beginning of the intestinal tract. These efferent bile ducts are lined by columnar epithelium varying in height according to the caliber of the duct. The larger ducts are supplied with unstriped muscle fibers, chiefly longitudinal, and small mucous glands. At the terminal portion of the common bile duct, in that portion that runs obliquely between the coats of the duodenum, this unstriped muscle becomes augmented into a definite circular bundle, which Oddi described, and which acts as a sphincter controlling the expulsion of bile into the intestine. Connecting with the cystic duct is a pear-shaped, distensible sac, the gall-bladder, which is composed of an outer coat of fibrous elastic tissue, a muscular coat, largely composed of circular bundles of unstriped muscle fibers, and a mucous coat covered with a single layer of columnar epithelium and thrown up into a network of slightly raised ridges that give the mucosa a reticulated appearance. At the neck of the gall-bladder may be found branched mucous glands.

That the gall-bladder has a function has recently been disputed, especially by surgeons, but if it has a function—and I, for one, believe it has—it primarily consists of acting as a reservoir for the bile secreted by the liver, which dripping down the bile ducts encounters a closed sphincter, and which has no outlet except to dam back through the cystic duct and into the gall-bladder. Here it remains stored for a variable time, becoming more concentrated,

until physiologically the sphincter of the common duct is relaxed, as a spurt of gastric chyme enters the duodenum; then bile is poured into the intestine in quantities suitable to the needs of the elements in the food to be digested, and here is where the secondary role of the gall-bladder function comes into effect. It is a well-known fact that a gastric chyme rich in fats, proteoses and peptones, partly because the bile aids in their direct digestion and partly for other reasons, as it passes the duodenal mucosa stimulates an excessive amount of excretion of bile. This then the healthy gall-bladder is able to furnish in concentrated form and appropriate dosage, whereas a diet rich in carbohydrate in whose digestion the action of bile is less concerned does not cause as copious excretion of bile; but the carbohydrates need pancreatic juice, which is delivered through the relaxed common duct sphincter together with such quantities of bile as may lie in the ducts. In this type of diet it is altogether likely that the gall-bladder does not play such a prominent part.

Prolonged periods of quiescence on the part of the gall-bladder—waiting for its physiological stimulus of fats or end-protein-products of gastric digestion—should logically predispose to biliary stasis.

It would be interesting to ascertain the relative frequency of functional (?) biliary stasis and later biliary disease occurring in people who have adopted a vegetarian dietary. This would help to settle the question. Similarly, it would be interesting to learn the liability to biliary stasis and gall-bladder disease occurring in men who for some years have worked under pressure, and have either missed the noonday meal or have hastily eaten a piece of pie or shredded wheat biscuit and glass of milk—a characteristic lunch of the busy business man or doctor during his foolish formative years. I can think of several such doctors who are today minus their gall-bladders.

Now let me pick up some of the loose ends and partly recapitulate. We see that physiologically the biliary system consists of an organ (the liver) which is probably constantly secreting bile, but is excreting it intermittently into the intestines. The function of excretion is controlled by the physiologic opening and closing of the sphincter which guards the outlet of the bile-conducting tubes. When this sphincter is closed it is probable that the secretion of the liver slows down somewhat, but it is also most probable it does not cease altogether and that the bile secreted passes down the ducts to find the sphincter closed, and having no other outlet the excess bile dams back into the gall-bladder—which has wisely been placed in the proper position to act as a reservoir for such an overflow. Is it not probable that the gall-bladder has been provided with an outer fibro-elastic coat to permit of variable degrees of distensibility? It is true that the velocity or rate of liver secretion varies in response to substances brought to it in the blood (and possibly through nervous influences), for Bayliss and Starling have demon-

strated that an acid gastric chyme on reaching the duodenum activates prosecretin into secretin, which is carried to the liver by the blood and stimulates its secretory activity, in a similar way in which these same hormones influence pancreatic secretion. It is my opinion that there may be a hormonic influence that passes to the gall-bladder itself which, independently perhaps of that inducing increased velocity of liver secretion, causes the gall-bladder to contract and deliver various amounts of its concentrated bile, and that this selective hormonic influence may lie in the *food chemistry* (proteoses and peptones) of the acid gastric chyme. For I, as doubtless many other observers, have been impressed with the inferential diagnostic importance, in patients with the biliary syndrome, of the low subacid or anacid fractional gastric curve, as pointing to biliary stasis with cholelithiasis rather than to cholecystitis alone. In my experience the cases of cholecystitis are more liable to show a normal or hyperacid fractional curve not unlike that seen in the majority groupings of duodenal ulcer and chronic appendicitis with reflex gastric symptomatology.

Now upon what does the mechanism of emptying, partially or wholly, this biliary system, depend? We can look for the answer to this by examining into the nerve supply of the duct sphincter and of the gall-bladder.

Doyen has specially studied the innervation of the gall-bladder, and his experiments were confirmed and amplified later by Freese. Both have shown that the gall-bladder receives both motor and inhibitory fibers by way of the splanchnic nerves, which emerge from the spinal cord in the roots of the sixth thoracic to first lumbar and pass to the celiac plexus.

Sensory fibers capable of causing a reflex constriction or dilatation of the gall-bladder are found in both the vagus and the splanchnic nerves, and it is found that stimulation of the (*a*) central end of the cut splanchnic causes a dilatation of the gall-bladder (reflex stimulation of inhibitory fibers); (*b*) central end of vagus causes a contraction of gall-bladder, dilatation (inhibition) of the duct sphincter. It is probable that the afferent fibers run in the vagus.

Conversely, stimulation of the peripheral end of the splanchnic nerves in the duodenum and the common bile duct causes simultaneously a relaxation of the tonus of the duct sphincter and a contraction of the gall-bladder.

Thus we find a double innervation of antagonistic or crossed action, which Meltzer calls "contrary innervation," and around which he has formulated a "law of cŏntrary innervation," which he not only applies to emptying the gall-bladder but which he finds holds true for many functions of the animal body.

Meltzer draws an analogy between the biliary and the renal system. The latter is made up of a constantly secreting organ, the kidney, passing its secretion down a series of tubes guarded at their outlet by a sphincter muscle with a distensible sac, the urinary

bladder, placed between the two. Owing to the double and contrary innervation of this system, when we wish to empty the bladder we contract the detrusor muscle of the bladder and inhibit the tone of the sphincter urinæ, and when the urine has been expelled the process is reversed, the sphincter contracts and the detrusor muscle becomes relaxed until sufficient kidney secretion has accumulated to fill or partially fill the bladder again when the act is repeated. This, of course, in health is a voluntary action, whereas the emptying of the biliary system is entirely independent of the will—otherwise the analogy is complete. Would that we were given a consciousness of an overdistended but otherwise healthy gall-bladder and could empty it when we wished, for then many of the diseased states of the gall-bladder, which we are now called upon to diagnose and to treat would be forestalled. But Nature has left the solution of this secret for our present and future endeavors. Possibly we are nearer the threshold of discovery than we think.

Now to make my hypothesis more understandable let me quote from Meltzer's article at some length. He says:

"While the physiologic muscular and nervous mechanism of bile storage and bile discharge is thus satisfactorily explained, the question presents itself: What are the causes that bring about either of the two actions? We compared the mechanism of the gall-bladder with that of the urinary bladder. But the latter is to a large degree under the management of the will, and the sensation of fulness and other sensory stimuli bring the condition of the bladder to the attention of our consciousness, which, by means of the will, sets the required part of the mechanism into action. The processes of storing of the bile or of emptying it never comes to our consciousness and are never managed by our will. What does then manage their proper activity? We must admit that we do not yet know a great deal about it. It is probable that certain conditions and certain substances exert a selective action upon the reciprocal reflexes. It is interesting to quote here some newer instructive statements. One comes from Pavlov's school. Bruns stated that no bile appeared in the duodenum as long as the stomach is empty—when a meal is taken the entrance of chyme into the duodenum gives the signal for an ejection of bile from the common duct. Most interesting are the recent studies of Rost. He first established the fact that after *cholecystotomy* the escape of bile through the papilla of Vater is indeed continuous, while in normal animals it is a discontinuous one, depending upon the entrance of food into the duodenum. He found, further, the instructive fact that injection of peptone or albumosis through a duodenal fistula in a normal dog causes immediately a discharge of bile from the common duct, and he has proved that this takes place by a reflex act which causes a contraction of the gall-bladder and simultaneously a relaxation of the sphincter of the common duct.

"From the foregoing it seems quite safely established that the

physiologic discontinuous character of the flow of bile into the duodenum is regulated by a reflex mechanism, dominated by the law of contrary innervation; that the integrity of the gall-bladder is an important part in this reflex mechanism; that the discharge of bile can be greatly curtailed by the absence or a restriction of the discharge of chyme from the stomach into the duodenum and that the discharge of bile through the papilla of Vater into the duodenum is greatly enhanced by the presence in the lumen of the latter of peptone or albumosis."

It is probably beyond controversy to say that the physiologic mechanism of the storage and discharge of bile is a reflex mechanism. It remains for the future to decide how much of it is a direct reflex (gastric chymes, etc.) and how much indirect, due to hormonic action. It is certain that both of these factors, and possibly others, enter into the complete physiologic mechanism.

Now, then, the hypothesis upon which I have been working frames itself around the fact that Meltzer (reinforced by the observations of Rost) found that by douching the duodenum *locally* with magnesium sulphate he could relax the duodenal wall and probably with it the sphincter of the common bile duct. This was all he said, but arguing from cause to effect it seemed evident that if his law of contrary innervation were a sound one, when the sphincter was inhibited the gall-bladder should be stimulated to contract and should empty its contents (wholly or in part) into the duodenum, and by means of the duodenal tube the bile could be collected into bottles for study. This was by no means difficult to verify, and after a few observations the practical possibilities of this very simple method of examining into the diagnosis of many of the biliary diseases was quickly seen. And later, as I have gone on with my observations, there has dawned on me a very attractive vista of future possibilities, particularly in regard to treatment by this method if only I can "get it across" to the profession in general, and if I can stimulate others to study into its practicability.

And now I have come to a point in my paper where, with this preliminary understanding of the question I am discussing, I can again put on record the observations which I published in my earlier papers[5 6 7 8] on this subject and to which I will ask you to refer for the details that time does not now permit me to enter into. And without coming to definite or hasty conclusions myself, I will ask you to examine carefully the sequence of findings in a non-surgical gall-bladder tap and by your critical discussion of them help to put a correct interpretation upon their meaning.

When a duodenal tube is passed through the pylorus of the stomach, during its interdigesting or fasting period, it should find

[5] Lyon: Jour. Am. Med. Assn., September 27, 1919, lxxiii, 980.
[6] Lyon: Am. Jour. Med. Sc., April, 1920, clix, 503.
[7] Lyon: Med. Clinics of North America, March, 1920, iii, 1253.
[8] Lyon: New York Med. Jour., July, 1920, Nos. 1 and 2, cxii, 23 and 56.

in states of health the sphincter of the bile duct closed and the duodenum free of bile; but within a few minutes after irrigating the duodenal mucosa with a solution of magnesium sulphate of various strengths it will be possible by either gravity drainage or by gentle vacuum suction to recover bile, indicating that the tone of the sphincter of the common duct has been inhibited, its walls relaxed and that by the *vis á tergo* in the biliary apparatus the bile is being forced into the duodenum.

There should be little argument over the statement of my belief that the first bile collectable should be coming from that lying within the ducts themselves, and especially of the common duct, since it is obviously the first source of supply. To relax the common duct I have for the most part used a solution of magnesium sulphate varying from 12.5 per cent. to 50 per cent. of a saturated solution in amounts between 50 to 100 mils. It has seemed to me that the stronger solutions of 25 to 37.5 per cent. have given an optimum amount of sphincter relaxation which lasts from a period of one to two hours. Through the glass window cannula placed about eight inches from the proximal end of the tube can be observed the changes in color, viscosity and gross abnormal elements in the bile being recovered and which can be received into separate receptacles for differential study by attaching sterile vacuum bottles.

The first bile collected is usually diluted with a few milliliters of the magnesium sulphate solution, but its color gradually deepens until it becomes apparently a pure bile of a light golden-yellow color and of medium viscidity, like that of syrup, and in healthy bile ducts perfectly transparent (with a certain exception to be mentioned later). After a few milliliters of this bile have been withdrawn (which varies, perhaps, from 10 to 30 mils.) the bile suddenly deepens to a considerably darker golden yellow and becomes noticeably more viscid, and usually transparent in healthy states, draining sometimes steadily, sometimes with slight intermittency until amounts have been recovered which have varied from 30 to 166 mils., within my personal observations, when a sudden transition in color and viscosity of the bile again appears, this time to a light transparent lemon yellow and distinctly thinner and more limpid than either of the former types, and this type of bile continues to flow with considerably greater intermittency as long as the relaxation of the common duct sphincter is maintained; the amount of this last type of bile recovered has varied from a few milliliters to several ounces. Now I will ask you the question, Where is this darker colored bile in the amounts of from one to five and a half ounces coming from? It is my personal belief that it is coming from the gall-bladder wholly or in part, but mixed, probably, with a few milliliters of bile still delivered from the ducts or bile freshly secreted from the liver. This is really the central point of this paper. Is this darker colored bile coming from the gall-bladder?

My reasons for believing it is derived in large part from the gall-bladder itself are four:

1. Because I believe that Meltzer's law of contrary innervation as applied to the biliary apparatus is a correct one and is based upon a sensible interpretation of the most probable mechanism of the physiological storage and discharge of bile, supported by the experimental observations already recited, and which I have had opportunity to confirm by my clinical experimental studies. Now, if this law of contrary innervation as applied to the biliary system is a tenable one, and if the action of magnesium sulphate serves to relax the tonus of the sphincter of the duct, then it must also serve to contract the gall-bladder walls and cause it to expel its contents, wholly or in part, depending on the one hand on the tonicity possessed by any given gall-bladder wall and upon whether its cystic duct is patulous, and on the other hand upon the length of time in which the impulse to gall-bladder contraction and sphincter relaxation continues to be maintained.

2. My second reason lies in the fact that the color and viscosity of this second bile indicates a higher concentration and strongly suggests it as coming from its storage chamber within the gall-bladder; that in certain pathological cases (cholecystitis and high grade biliary stasis) this bile is a thick, sometimes almost tarry, greenish-black, of the consistency that we have all of us seen scooped out of the operated gall-bladder; that its cytology in health, but far oftener in diseased states, shows a larger amount of desquamated columnar epithelial cells deeply bile-stained, as if they had lain in contact with concentrated bile for some time. On occasions I have recovered bile-stained columnar epithelium in such massed abundance that they gave a ridged appearance, such as the reticulated folds of the gall-bladder mucosa possesses. Furthermore, in cases of clinically suspected cholecystitis it is in this second bile that appear by far the larger number of mucopurulent flakes, rich in pus cells and inflammatory debris and often swarming with bacteria, and lastly because the microscopy of this second bile finds normally the larger deposition of bile crystals. In several calculi cases that have been operatively (or otherwise) confirmed, bile crystals occurred in such abundance as to give a gritty or sandy feel to the bile when rubbed with the finger. This observation, together with one other that I shall mention later, offers the most practical differential inference as to the presence of potential or present cholelithiasis.

3. My third reason for believing that this second bile is derived largely from the gall-bladder lies in the fact that unless we account for it as gall-bladder bile we must account for the presence of from one to (in certain cases) nearly six ounces of this darker colored and more concentrated bile as coming from somewhere between the common duct sphincter and the secreting cells of the liver. Now, how much bile do you suppose the common and hepatic ducts can contain in their total length of $8\frac{1}{2}$ inches and their average diameter of $\frac{1}{4}$ inch? Surely it is unlikely that they could hold 90 to 150 mils.

At any rate, if this second bile is *not* from the gall-bladder the burden of proof will rest with the opponents to my theory as to whence it is derived.

4. My fourth reason, and I feel it is the strongest, for believing that this second type of darker yellow and more viscid bile is actually coming in large part from the gall-bladder lies in this (I think) convincing fact, namely, that in the cholecystectomized patients that I have studied postoperatively, some ten or more cases, I find, (*a*) that I never recover the second type of dark bile[9] but pass immediately from the light golden yellow or relatively more concentrated common duct bile to the light lemon yellow and limpid bile that I believe is freshly secreted liver bile and collectable for long periods as rapidly as it is secreted, and (*b*) I find that (in this cholecystectomized group) in the larger number of instances bile is continuously entering the duodenum in the fasting stomach and duodenal state, indicating that the duct sphincter is in a state of inhibited tonus, probably permanently so, since the antagonistic or contrary innervation has been cut when the gall-bladder was removed.

5. I might add a fifth reason, to the effect that in my post-operative group of cholecystostomized patients upon whom this non-surgical method has been practised (because the length of time over which surgical drainage could be maintained has not been sufficient to allay the catarrhal inflammation or to arrest the infection), that is in this group, together with a group of non-operated patients with cholecystitis or with gall-bladder biliary stasis, I have seen this second type bile, easily demonstrable as pathologic, gradually clear up and return to a more normal appearance under biweekly drainage by this method.

A little while ago, I made the statement that within my observations I find the bile, always in states of health, and indeed in certain states of disease (*e. g.*, infective cholecystitis of low grade without producing a recognizable catarrhal inflammation, and in certain types of biliary stasis) of a transparently clear yellow color with one exception. This exception occurs when a spurt of gastric acid juice enters the duodenum and mixes with the bile being collected, when an instantaneous turbidity is produced, the microscopy of which reveals a precipitate (?) of lecithin, neutral fats, mucin and occasionally other elements which, as yet, I have not identified. The density of this turbidity varies apparently in direct proportion to the concentration of gastric acidity. It can be artificially produced in almost every specimen of bile by adding to it a few drops of dilute hydrochloric acid, a 0.5 per cent. solution causing a very dense turbidity.

[9] It is conceivable that in cases in which the gall-bladder has been removed, and in which the ducts remain infected and the common duct becomes secondarily obstructed, that in such cases dark, inspissated or static bile might be recoverable.

I wish, too, at this point to state the second observation that may help in the differential diagnosis of cholelithiasis by direct study of the bile (in addition to the gritty feel of some biles due to excessive crystalline precipitation), and it is this that occasionally when a spurt of gastric acid juice reached the duodenum, besides causing the aforesaid turbidity it creates an *effervescence* that is quite noticeable and continues for some time. It resembles closely the reaction seen in the urine containing carbonates on adding acetic acid, and suggests the possibility of detecting in the bile a carbonate (or phosphate) diathesis which may be concerned in calculi formation of the calcium variety. This point I believe will bear watching in the future. I have not encountered this turbidity of bile in cases in which there is gastric anacidity or achylia, nor so frequently, or with such a dense turbidity in those cases having gastric subacidity, and since it is in just this group of gastric curves that the chief diagnostic relationship to cholelithiasis lies, I would make the suggestion that in all cases the bile being studied should be artificially acidulated with hydrochloric acid and the resultant turbidity microscopically and chemically investigated.

I hope by now I have made clear the reason why I believe the general hypothesis upon which I have been working is sustainable and that you will now more fully appreciate the reasonableness of my arriving at certain conclusions in regard to whose tenability I solicit your critical weighing of the evidence I have put before you. It sums up into this, and brings me back to one of the early paragraphs of this communication, namely, that by this method of direct (hormonic ?) stimulation of the contrary innervation of the gall-bladder and the duct sphincter I believe it is possible to drain the biliary system, to actually empty the gall-bladder, partially or wholly of its *fluid* contents, and to segregate the several biles recovered (somewhat roughly I admit) in such a manner as to make it practically possible to make certain differential diagnostic inferences as to the state of health or disease of the several components of the biliary system in a scientifically correct manner not hitherto attainable. I shall have to ask you to refer to my four former papers[5 6 7 8] for a *résumé* of the possible diagnostic inferences, and later on I shall bring my diagnostic observations up to date.

Now if I have presented my argument sufficiently clearly, and if it can be temporarily admitted, and perhaps definitely proved in the future (and I shall have some suggestions to offer later as to how this direct proof can be obtained) that it is possible not only to drain the bile ducts and the liver of its secreting bile, but also the gall-bladder itself, then I need not now do more than to direct your attention to the possibilities that this method opens up for the treatment of various biliary states that heretofore have been best attained by purely surgical methods and to stimulate your enthusiasm for investigating into the precursory and probably functional states of biliary disorders of motor, secretory and nervous origin

which, if allowed to continue, will almost invariably lead to inflammatory, infective or calculus-forming states of disease.

In my opinion the most hopeful feature of this method lies in its practicability of investigating, by clinical experimental observations, in the attempt to detect some of the physiologic alterations of *function* of the gall-bladder, liver and ducts; disorders of function, such as the hitherto undescribed entity of functional atony of the gall-bladder; spasm of the ducts and lowered velocity rates of liver secretion, which directly contribute to slowing up the excretion of bile and bring about biliary stasis.

For it is biliary stasis that all writers are in agreement as being the forerunner of gall-stones and of inflamed and infected gall-bladders and gall ducts. Any successful method of directly determining biliary stasis immediately opens up fields of investigating and explaining such common conditions as we loosely call biliousness, liver lethargy, hepatic torpor, with their resultant migraine and migrainoid attacks with biliary vomiting. Permit me to quote from another article[10] I have recently written: "If we are to attack the great problem of gall-bladder disease, gall-stones and gall-bladder and duct catarrhs and infections, and attack it at its source, we must give this lightly passed over symptom-grouping called "biliousness" our serious attention. Thus far our attitude toward the gall-bladder problem has been one of *correction* of the full-blown stages of formed calculi and active catarrhal infection, and the means adopted have been largely surgical. The surgeon's achievements in pioneering this subject have been very great. Their results have been at times brilliant, often less satisfactory and not infrequently bad, requiring many and repeated surgical maneuvers usually eventuating in that *bête noir* of surgery, distorting post-operative or postinflammatory adhesions, so that the state of chronic invalidism of the patient is a heavy cross to bear. What we must do is to attack the problem with methods of *prevention* of gall-bladder disease, with its sequelæ, and this brings us back to attacking the biliary stasis which is at the root of the matter. Biliary stasis is followed by overdistention of gall-bladder and ducts, leading perhaps to what we may designate in the future as gall-bladder atony. This engenders catarrhal states of gall-bladder and duct mucosa, weakening resistance and permits of successful implantation of infecting microörganisms, filtered out from the portal blood or carried directly to the gall-bladder by the systemic blood or by the lymphatics, or ascending to the gall-bladder by way of the duodenum and the common duct or passing through the serosa of the gall-bladder from direct contact with contaminated peritoneal coverings of neighborhood viscera. Biliary stasis, with its concentrated bile and precipitation of its crystalline chemistry, plus catarrh, plus infection, means gall-stones. Therefore it is

[10] Lyon, B. B. Vincent: Some Aspects of the Diagnosis and Treatment of Cholecystitis and Cholelithiasis, Medical Clinics of North America, March, 1920.

biliary *stasis* that we must attack if we are to prevent gall-stones, catarrhs or infections."

Can we do so? I think we may entertain greater hopes of so doing if wide application can be made of this method of investigating into some of the predisposing factors and conditions that we know enter into the precalculous and preinfective states of the gall-bladder and ducts. I would suggest that the problem be attacked first by a careful clinical study of that large group of individuals who have periodic or cyclic attacks of so-called "biliousness," or "lazy" liver, ushered in by gradual loss of ambition, increasing sense of mental and physical heaviness or lethargy, constipation, furring of tongue, metallic sense of taste, loss of appetite and headaches and eye-aches of greater or less severity; many attacks terminating in the true migraine type, accompanied by nausea and vomiting, various ocular manifestations, dizziness and various degrees of prostration, a group of symptoms that in some degree we meet within our practice nearly every day. These patients usually find out for themselves that their complaint is best relieved by calomel or other of the so-called cholagogic group of medicines, and they learn, furthermore, that they are rarely cured by such means. Various pharmaceutical houses, to say nothing of many independent pseudo-doctors, have made fortunes, as well as paid for a lot of expensive advertising and literary propaganda, from exploiting this very common symptom-complex, advising this or that laxative pill or liquid medicine, which at best gives only a modicum of temporary relief.

I surmise that it will surprise many of you to recover from such patients four ounces of more static bile from a gall-bladder whose normal capacity all anatomists agree in limiting from $1\frac{1}{2}$ to $2\frac{1}{2}$ ounces. When such amounts are recoverable I think it reasonable to assume that such a gall-bladder is being stretched beyond its physiologic limits of distensibility, and if this stretching is continued such a gall-bladder loses its normal tonicity of contraction and the organ becomes functionally atonic (as does any other hollow and distensible viscus, such as the stomach, the colon, the bladder, etc.) and is physiologically incapable of emptying its contents completely. In the future we may be able to speak of such gall-bladders in terms of "residual bile," as we now are quite accustomed to the term of residual urine in the domain of the urologists. I hazard the prediction that in the future the duodenal tube may be used quite as easily and freely, and certainly far more painlessly, to empty such distended gall-bladders as the urinary catheter is used today. And no thinking doctor of today would dare challenge the statement that such functional(?) disorders of the gall-bladder do not have a most important bearing on the production of later and more serious gall-bladder diseases.

I see no great difficulties in studying by this direct means the clinical-pharmaceutical action of the whole series of so-called chola-

gogues (and such a study is already under way) by both directly douching the duodenum with these drugs in solution and by allowing them to be swallowed and passed through (or absorbed by) the stomach and note the rate and amount and type of biliary discharge. The same method of study can be paralleled in investigating the recent pharmaceutical preparations designated as hormones to stimulate pancreatic secretion and the recovered mixed bile and pancreatic juice can be studied for pancreatic efficiency. Similarly the group of antispasmodics, atropin, belladonna, benzyl-benzoate can be investigated, as well as the effect of Witte's peptone or of egg albumen subjected to preliminary artificial gastric digestion, and of various meat extracts and extractives.

There are unbounded avenues of investigation waiting to be taken up, all of which will have a direct or indirect bearing on solving the great problem of gall-bladder disease, namely, the prevention of biliary stasis and thereby that of cholelithiasis.

One very practical field of usefulness came to my attention at the Methodist Hospital during my summer service. Several fully convalescent typhoid patients were retained in the hospital because their cultures from either urine or stool still came back "positive for typhoid bacilli," and they could, therefore, not be discharged on account of the danger of becoming "carriers." Several such patients were found to be harboring typhoid bacilli in their static gall-bladder bile. This is the time to treat such a case by non-surgical drainage, and that patient may not need to be operated upon several years, or even decades later for the removal of gall-stones from whose nuclei the pathologist may report the bacteriological recovery of a pure culture of the Bacillus typhosus, as has happened quite frequently in the past. I would suggest considering the advisability of testing directly the biliary excretions of all convalescent typhoid patients, both to prevent their becoming "carriers" and to guard them from later developing more serious gall-bladder disease.

One good reaction, as the pendulum swings from one extreme to the other, I am sure many of us have welcomed as being a rational one, and that is to stop starving our typhoid cases as we used to do ten to fifteen years ago and to start feeding them on a sensible dietetic plan as advocated several years ago by Coleman. Since this plan of feeding has been more widely carried out we have seen fewer instances of a complicating typhoid cholecystitis, for the simple reason that we are now giving the patient food mixtures that produce an acid chyme capable of changing proteids into proteoses and peptones and thus deliver to the duodenum a food hormone that permits the duct sphincter to relax and the gall-bladder to express its static bile. I think this point is worth considering also in connection with the dietetic management, assisted by artificial gastric juice, in those subacute and chronic infections of long standing that tend to create a state of gastric subacidity.

For similar reasons in treating my selected medical group of duodenal ulcer cases (the non-obstructive type, etc.) by duodenal feeding I am draining their gall-bladder once a week to prevent the bile from becoming static during that three or four weeks period in which the duodenum is deprived of the food-bearing acid gastric chyme which acts as one of the physiologic reflex agencies for bile discharge.

This is the best place to refer to the natural limitations of this method and to the fortunately small group of diseased states of the gall-bladder and ducts in which it is probably impossible to empty the gall-bladder. I refer especially to those cases in which the cystic duct is obstructed, although this may prove to depend somewhat on the nature of the obstruction and upon the relative tonicity remaining to the gall-bladder. I do not believe it will be possible to empty the gall-bladder when a calculus is embedded in the swollen and congested lumen of the cystic duct, although Nature has, in times past, accomplished this even when unassisted. It will be impossible, naturally to empty the gall-bladder when this duct is mechanically obstructed by inflammatory adhesions or when an enlarged lymphatic gland alongside of the cysticus obstructs it by direct mechanical pressure, as Deaver[11] called our attention to some years ago. Nor do states of hydrops, due to swelling of the mucous glands at the neck of the gall-bladder, offer much better chance of success, and certainly not when a mass of calculi make a stony cast filling the entire lumen of the gall-bladder sac.

The practical value of this method, so far as it concerns treatment, is that it adds greatly to our medical armamentarium in treating all of the recognizable early states of biliary stasis, many of the later states of biliary stasis as seen in patients with atrophic gastritis (often preceded by oral sepsis), with pernicious anemia, with certain forms of auto-intoxication and that large group presenting symptoms of both early and late migraine states. I have already reported my results in treating simple catarrhal jaundice in which I was able to reduce the duration of the disease by 52 per cent. in one group of patients as compared to a second group treated by the customary symptomatic or expectant plan, and I have learned, through personal communications, that other doctors have since had even greater success with the method.

I believe that by this method we can adopt in a non-surgical way the generally accepted surgical principles of free drainage as applied to some of the early catarrhal and infective conditions of the biliary tract, and I believe do it thoroughly and effectively, with a far better check on how effective it really is and with an avoidance of certain definite surgical risks. It cannot and need not supersede surgery—the very necessary surgery—for the removal of calculi, for the drainage of acute or chronic empyema, for the removal of

[11] International Clinics, vol. i, eighteenth series.

the gall-bladder in gangrenous cholecystitis or when its wall or lymphatic glands are the seat of a chronic focus of infection, or of carcinoma, or for the relief of mechanical obstructions produced by adhesions, although it might be well used to *supplement* some of these operations and to further ultimate recovery of the patient. The physiologic mechanics of this method should appeal to the surgeon, and therefore what I had said in this paper need not offend the minds of those who think only from the surgical-mechanical angle that nothing is good or worth while doing unless it is done by means of the aseptic scalpel, and who continue to teach suffering humanity that the only royal road to health is by the "cut well, sew well, get well" route. I am not so sure that by the dead pathology of the autopsy room or by the living pathology as seen at the operating table we have obtained the complete picture of many diseases; we have caught the full-face view, but I feel convinced that we have missed many of the profiles, to say nothing of the full-length multiple-mirrored reflection. During the past two or three decades we have learned much of the later life history of disease. The development and extensive use of the microscope applied to examining in closer detail our autopsy material has taught us many facts of dead pathology. The wonderful accomplishments of surgeons during this time by their marvelous dissection and removal of diseased tissues have taught us much of the living pathology of those earlier stages, that if uncorrected speed on the lethal end. It is true that we have been taught the characteristic lesions that diseases, if left unchecked, can by their very nature produce; but let us take a bird's-eye view of what has been accomplished in the past decade by that relatively small but brave band of physiologists who have come on with the giant stride of the seven league boots, and I opine that the wise doctor of the future will be he who with open mind can grasp the accepted facts of experimental physiology and by practical use of physiologic principles assist Nature to help herself. Not that we have not done much to correct by our increased knowledge and skill pathologic lesions, but that we should do still more to prevent them.

I confess, too, to have lost my enthusiasm for and my belief in the infallible diagnostic acumen of the intuitive genius who by simple touch of the "educated" finger can say that this patient has a chronic cholecystitis and that one a chronic appendicitis, and thereupon proceeds to remove the perhaps unoffending organ on the ground that its physiologic function is aborted or that it harbors a pathogenetic factor that menaces future health and leaves instead the too-often postoperative adhesion or the incisional hernia. Heaven knows that my dispensary clinic is only too full of the results of such faulty diagnosis and injudicious surgery.

And I find it difficult to believe that the trained master of living pathology can always tell by practised eye and touch that this gall-bladder, with its somewhat thickened and shrunken wall, is physio-

logically incompetent and incapable of resuming its function and make a bull's eye every time. A critical review of Case No. II will serve to support this contention.

You will see, then, that I am presenting this method of physiologically draining the gall-bladder (1) as a *means of diagnosis* of biliary diseases to supplement the usual clinical methods of diagnosis and the great help given us in many cases by the roentgenologist; (2) as an *alternative method of treatment* of many types of gall-bladder and duct disease in which there arises a question of opinion as to whether surgery is or is not emphatically and immediately indicated, and (3) as a *supplementary method* of postoperatively continuing the surgical principles of drainage in those cases incompletely cured by surgical measures alone.

To present the merits of this method of diagnosis and treatment it is clearly necessary that I submit for your inspection a few case reports of patients so treated, and to this end I ask your indulgence for a few minutes longer. These case reports have been selected for the purpose of illustrating different points contained in the subject-matter of my paper. I have many others that would serve equally as well.

The first case I am presenting was the very first patient of my series and illustrates what can be accomplished by this method postoperatively in treating acute choledochitis.

Case I.—Miss A. I., aged seventeen years, was suffering with an infection of the common bile duct, with inflammatory swelling causing an obstruction of the duct. It had been essentially a chronic condition for two years, with intermittent acute exacerbations. This patient had had three major gall-bladder operations and two minor operations performed upon her in three years. The first one at the age of twelve years. In addition to this she had had six other admissions to the same hospital on both the surgical and medical services for non-operative measures for postsurgical sequelæ and had been treated by bed-rest, external applications, urotropin, the salicylates, morphin, codeine, sodium phosphate, nux vomica, cascara, calomel and other drugs, and was given various modifications of her diet, with at best only palliative effect.

At the end of this time she still had an infective choledochitis which was subject to acute remittent exacerbations of the most characteristic type. During the early spring of 1917, while in an acute attack, the surgeons in charge transferred her to me.

At that time she was definitely septic (of the chronic type), undernourished and intensely jaundiced. She had a leukocytosis of 17,000 to 26,000 with low polynuclear resistance. She was suffering intensely with acute paroxysmal upper abdominal pain and persistent nausea and vomiting. The muscles of her upper right quadrant were rigid and exquisitively sensitive to both light and deep palpation. In short, she presented the picture of a case that would be considered clearly surgical were it not for the fact

that she already had had her gall-bladder drained for an acute empyema. Six months later her gall-bladder was removed and her common duct drained. One year subsequently the common duct was again drained and several small stones were removed from the common duct, stones which had probably formed in the duct as a result of biliary stasis, associated with the persistent common duct infection and obstruction. The surgeons had still vivid recollections of the difficulties encountered in the last two operations of exposing the operative field on account of the dense mass of inflammatory adhesions.

This, then, was the first patient upon whom this direct non-surgical method of drainage was attempted. I am citing this case in some detail to direct attention (1) to the fact that it was certainly not the type of case in which one would expect much success from a new and untried method of treatment and (2) that it resulted in a most successful outcome.

This patient's obstructed common duct was unplugged by the local douching of the duodenum by magnesium sulphate and by the use of hot bland inflammation-allaying solutions of boracic acid and Ringer's salt. In this case I believe the unplugging of the duct was more directly due to the effect of the latter two solutions, but I used the magnesium sulphate because I had just read Meltzer's article. On relieving the duct obstruction I recovered infected pathologic bile containing pus cells, inflammatory debris, crystalline pigments and bacteria. The B. pyocyaneus was isolated in pure culture from this bile. Incidentally it is of interest to note that this same organism was recovered from bile discharged from the abdominal sinus following her first operation five years earlier, and had doubtless persisted as the infecting agent, notwithstanding a thorough course of autogenous vaccination.

After the common bile duct had been unplugged it was kept open by continual duodenal-tube drainage for several days, with direct disinfection and cleansing of the duodenal zone with potassium permanganate and normal salt solution three or four times a day and duodenal feedings every fourth hour. After one week of this, biliary drainage for two hours, followed by duodenal disinfection, was practised every second day. By the third day following the inauguration of this direct method of treatment the critical picture of this patient had very materially improved; the paroxysmal pain subsided with the establishment of biliary drainage, the septic temperature dropped, the muscle rigidity relaxed, the intense jaundice lessened, the leukocytosis, which rose during the first three days from 17,000 to 26,000, gradually dropped. During the next four weeks there were several mild but never severe exacerbations, and from then onward her recovery was uninterrupted. By the ninth week the cultures from the bile which had continued to show the B. pyocyaneus were for the first time reported free from this organism. During this stage of her treatment and later she

was given a second long course of vaccination, which was carried on for two and a half months up to dosages of 3,000,000,000. During the next eighteen months she had two slight exacerbations, and on my return from France she reported herself at my clinic and was quite a changed girl; she had gained fifteen pounds in weight and had for the first time in my observation some natural color in her cheeks and a continued absence of jaundice. Besides, her acne, which was the worst I have ever seen, was very much improved. During this past year (1919) I have drained her common duct and irrigated her duodenum thirty-one times, partly because I have been using her case for some experimental work and partly because she has a fearful horror of a relapse, and because she states that she feels better after such treatments.

Her bile has been cultured several times this year and has been reported free from B. pyocyaneus. But to bring her case absolutely up to date for this paper I had her bile cultured three weeks ago and to my intense disappointment it was reported to contain B. pyocyaneus. I had been congratulating myself on her apparent absolute cure. I am somewhat easier in mind, however, to find that the larger colony counts are coming from her liver bile, and I suspect that she has a low-grade chronic infection of the liver itself. Under these circumstances, perhaps an absolute cure is too much to ask of any method of treatment. I believe, however, that her general restoration to such good health is in itself a most encouraging fact. Of course, a third set of vaccines have been prepared and will be carried through. This failure with vaccines, too, does not shatter my belief in their usefulness, for I have had too much assistance from them in the past. I shall continue to drain and disinfect her bile in the hope that final complete cure can be accomplished or at least will serve to ward off acute duct exacerbations.

I am very glad that this young woman has consented to let me present her so that you may see that her present state of health is very satisfactory. Of course, we should remember that her future health may be menaced with biliary obstruction on account of the many adhesions, happily no longer acutely inflamed, which still serve to distort the radiographic outline of her duodenum, and it is for this reason, too, that I shall continue to treat her duodenum with Ringer's and other solutions. With this and in keeping her bile draining as freely as possible lie the best chances of final success.[12]

I append the complete chronology of her case, with dates and diagnoses copied from the original records:

C. 1848. Oct. 5, 1912, to Oct. 31, 1912: Empyema of gall-bladder. Drainage.

[12] At this date of publication this patient is apparently cured, is working hard in a department store every day, and following five months of further biliary drainage and vaccine therapy no longer shows the presence of the B. pyocyaneus.

C. 3291. Jan. 6, 1913, to Jan. 11, 1913: Removal of tonsils and adenoids.

D. 6353. May 13, 1914, to June 8, 1914: Cholecystectomy and choledochostomy.

E. 500. June 23, 1914, to July 16, 1914: Repair of sinus from gall-bladder.

E. 6395. Apr. 16, 1915, to Apr. 22, 1915: Hysteria and cholangitis.

E. 7308. June 30, 1915, to July 10, 1915: Cholelithiasis (duct) and choledochostomy.

F. 1454. Aug. 12, 1915, to Aug. 26, 1915: Perigastric adhesions.

F. 3208. Oct. 27, 1915, to Nov. 8, 1915: Abdominal adhesions.

F. 6778. Apr. 15, 1916, to Apr. 22, 1916: Abdominal adhesions.

G. 707. July 3, 1916, to July 15, 1916: Surgical neurasthenia.

G. 4879. Jan. 9, 1917, to Mar. 5, 1917: Chronic cholangitis.

Methodist Hospital, April 2, 1917, to June 20, 1917: Acute cholangitis and duodenitis.

Treatment continued since April 2, 1917, up to present writing by method outlined in this paper.

CASE II.—This case, an operative one of cholelithiasis and cholecystitis, accurately diagnosed by this method and confirmed by the roentgenologist, had a cholecystostomy performed and surgical drainage for eleven days. It was found six weeks later, by this method, that he still had an infective catarrhal cholecystitis in which the identical group of organisms as those originally isolated were still recoverable. He has since then been treated postoperatively by physiologic drainage, with encouraging success. This is the first motive for reporting this case, and the second is to show that the operator cannot by visible and tactile observation of living pathology always tell the amount of physiologic function still left to a shrunken and apparently functionless gall-bladder unless it is completely fibrous. Some will say it would have been better surgical judgment to have resected this gall-bladder, on the grounds that its walls are probably the real source of the remaining infection. Perhaps so, but in that event this case might fall within my group of cholecystectomized postoperative cases who still continue to show evidences, clinical and direct, of infection. At any event it will be an excellent case to try out the merits of the method I am suggesting. I think it is well to bear in mind that the surgical principle of drainage in any case of cholecystitis depends for success upon how *efficiently* bile drainage can be secured and upon how *long* it can be maintained, plus the contributing effects of bed-rest and modification of diet. Whether or not the infection is cured (in the true as well as in the surgical symptomatic sense) will depend directly upon three factors: first the virulence of the infection, second the resistance of the gall-bladder mucosa and wall (as well as those of the ducts) and its capacity to recover from the effects of the infection, measured in terms of the third factor, the efficiency and duration

of the surgical drainage. After the surgical drainage tubes have been removed and the cholecystotomy wound has closed by adhesions or otherwise, *if the given gall-bladder has not been entirely relieved of its infection it is then left to Nature and to its own devices to do the rest.* The redevelopment of symptoms then becomes the apparent criterion of cure. It is here that the practical utility of this method for supplementary postoperative treatment becomes clearly apparent.

Protocol of Case II. Mr. J. H., a very robust man of forty-seven years, contracted influenza of the pandemic type, with bronchitis, in October, 1918. This was the only genuine infection of his entire life, although for twenty-five years he had suffered from chronic remittent attacks of migraine, which I believe may have been due to some degree of biliary stasis. His convalescence from the effects of the influenza was slow, and four months later he developed the first of five attacks of acute epigastric pain, colicky and cramp-like, followed by a dull aching and soreness, accompanied by vomiting, and during the last two attacks by jaundice of the mildest type. His stools were offensive and "gassy." During the four months' period of these attacks he had lost thirty-one pounds in weight. In none of the attacks was the pain ever referred to the back or to either shoulder, nor indeed even to the right hypochondrium.

Physical examination of his abdomen revealed *nothing* suggestive of gall-bladder, ulcer or appendix disease.

Examination of his stomach and duodenum revealed an infective type of anacid gastritis and duodenitis, and direct examination of his biliary system showed a pathologic "A" and "B" bile, the latter containing the greater abundance of mucopurulent elements, a swarming mixed bacterial flora and such an abundance of bile crystals as to impart a distinctly "gritty" feel to his bile. Cultures from "A" and "B" bile recovered the following organisms: B. coli, pneumococcus capsulatus, Streptococcus viridans and Micrococcus tetragenus. The recovery of three of this group of organisms strongly suggests the relationship of his gall-bladder infection to the preceding influenza with bronchitis.

A diagnosis of infective cholecystitis and choledochitis was made, with a suggested possibility of cholelithiasis, the latter being confirmed by the radiographic study of Dr. W. F. Manges. On account of the calculus state he was referred for operation. Sequence of events in his case:

Operation, October 16, 1919 (Dr. J. D. Elliott). Stomach and duodenum explored and declared surgically negative. No adhesions. Gall-bladder exposed and found shrunken and contracted, with thickened wall but no adhesions, and apparently it did not contain stones. However, on opening the gall-bladder it was found filled with a thickened greenish-black bile, similar to that of "B' bile, and between fifty and sixty small stones were scooped out, ranging between the smallest granules to large match-head size. The gall-

bladder was not removed (probably wisely) and rubber-tube drainage was sewed in with chromic gut. Surgical drainage was carried out for a total of eleven days. Postoperative recovery was uneventful.

Now, aside from the surgical removal of his gall-stones, was this man cured of his gall-bladder infection?

November 27, 1919. Mr. J. H. returned to me for reëxamination. Direct examination of his biliary system revealed "A" and "B" biles to be definitely pathologic, the latter containing a swarming bacterial flora, very many mucopurulent flakes which ran over 100 pus cells to the field, inflammatory debris, but a less evident deposition of bile crystals. Cultures from that bile recovered the identical group of four organisms as isolated before operation. Clearly then this patient had not been cured of his cholecystitis by the eleven days of surgical drainage.

Since November 27, 1919, he has had his biliary system physiologically drained by this method once a week, with gastric and duodenal disinfection, followed by transduodenal lavage with Ringer's salt or Jutte's solution, with steady improvement in the cytological findings, the mucopurulent shreds particularly have gradually decreased and the bacterial flora is less evident. He is being given, too, injections of an autogenous vaccine and is taking hydrochloric acid and pepsin and following an appropriate diet. This plan of treatment will be followed until ultimate cure is secured by the direct evidence shown in the cytology and bacteriology of his bile.

You will be interested to learn that this man's apparently shrunken and thickened gall-bladder wall is still capable of delivering bile under physiologic stimulation in amounts varying from two to four ounces. Certainly, the function of this man's gall-bladder was *not destroyed and gives promise of eventual restoration.*

To look at this gentleman as he sits before you, entirely symptom-free, with his good color and having regained his weight, no one would dream that he still had lurking in his gall-bladder a dangerous microbic infection capable of lighting up and producing further misehief unless carefully watched and controlled by this very simple and practical method.[13]

CASE III.—This case is reported because it illustrates what is possible of accomplishment in the treatment of biliary stasis, with low-grade infection of the gall-bladder and ducts, resulting in the severest type of migraine and evidence of early toxic arthritis. This may be called a "masked" gall-bladder disease, at no time giving rise to symptoms severe enough to warrant surgical consultation. Perhaps persistence in this method of treatment may result in true

[13] Since February, 1920, this patient has been treated at gradually lengthening intervals, and for the past three months has had a biliary drainage only once a month. Vaccine therapy has been continued. When last seen, on September 18, his biliary examination was quite normal. He has remained perfectiy well and, in his own words, "never felt better in my life."

cures in many of these cases, especially if caught early. Certainly the relief of symptoms after so many other measures have been unsuccessfully tried, entitles us to place high hopes on this method of physiologic biliary drainage combined with transduodenal lavage and the use of specially selected contributing measures to meet various angles of disorders and diseases, only brought to light by a searching diagnostic review of the various systems of the body. This case is also worthy of report to illustrate how the primary focus of infection may give rise to successive foci in the gastro-intestinal tract even though the primary focus itself has become quiescent or has disappeared; it also illustrates the advance of gastro-intestinal disease from one zone to another, with a corresponding transition in symptoms. Finally, this case illustrates the ease with which this method may be carried out, after a little preliminary instruction even in the hands of relatively unskilled doctors or attendants.

Mrs. "K.' was referred to me on August 27, 1919, by Dr. F. O. Lewis. She was forty-nine years old and married, with one daughter aged sixteen years, her only conception.

Her chief complaints were many, but in the order of importance to the patient were:

1. Headaches of great severity and frequent occurrence in cycles of variable duration.
2. Gas on the stomach, with nocturnal and diurnal cardiac palpitation.
3. Dizziness and light-headedness and easy fatigue.
4. General abdominal bloating, with wandering pinching and cutting, general abdominal pains, with sensations of "raw spots" in the abdomen.
5. Intestinal gas of offensive odor.
6. Obstinate constipation, if not daily prevented by laxatives, resulting in increasing laxative habit for fifteen years. Stools contain much mucus in the form of coarse shreds, casts and ropes, and stools are described to conform to type of spastic constipation.
7. Progressive loss of weight and strength.

Past Medical History: Measles, parotitis and pertussis in childhood, and since then has never been sick in bed except with "sick headaches," which have occurred with increasing severity and frequency.

Present Illness: She states that she has had "bilious headaches" ever since she can remember, many of them accompanied by sick stomach and occasional vomiting. For twenty-five years her headaches were associated with nausea and sour, gassy stomach, but about ten years ago the gastric symptoms disappeared and were replaced by lower abdominal bloating, cutting and pinching abdominal pains and increasing mucus in the stools, with increasing constipation punctuated by intermittent diarrheal periods. The headaches increased in severity, frequency and duration, and are described as follows: They begin as left orbital and pass to the

left temporal region—less frequently beginning in the right orbital region. They are very severe, usually putting her to bed; formerly lasting for eight to ten hours, for several months past they have lasted for two to four days. After the acute headache has stopped she will try to eat a little, and about two to four hours later gets a diffuse headache, with especially a sense of intense pressure on top of the head. She finds it is always worse after the head is exposed to cold or drafts, and so wraps her head in a hot woolen cloth, with some relief. Recently she has noticed that the bilious, sour stomach is not so noticeable a prodromal symptom, and has been replaced by pain in the arch of the left foot and under the toes, which become stiff and swollen and burn. The following day she wakes up with a sick headache. She says if she were not very careful with her diet she would have headache all the time; that she has not eaten any fried foods in nine years, because these always aggravate the headaches. She eats boiled meat (beef, lamb, chicken) with agreement, but thinks vegetables cause bloating and intestinal gas and increase the headaches. Tea and sweets also disagree. She states that for twelve to fifteen years she has been troubled with her teeth, with cavities and advancing pyorrhea, and that three months ago all of her teeth were extracted. She fights constipation all the time, because her headaches have been less when her bowels move freely, and she has occasional spells of diarrhea, with much mucus. She uses daily three to eight "pink laxative" pills and Pluto water. Her skin became sallow several years ago, but has become progressively browner and more bronzed. She has noticed progressive loss of strength and weight during the past eleven years, the later totaling 19 pounds, from 110 to 91. She has also noticed increasing depression and melancholia, and has been told that her case was "incurable." She has worn eye glasses for two years without any improvement in the headaches.

On Physical Examination: She presented the typical appearance of one suffering from a chronic intoxication or infection. Asthenic type. Thin, anemic, tired-looking, with dark circles under eyes and sallow brown complexion, with dry skin and thin, gray, dry, lusterless hair. Eyes: negative except for dilated pupils.

Nose, tonsils and glands are negative.

Tongue coated; gums clean and well healed and wears well-fitting double plates.

Dermatographia well marked. No typical Addisonian findings.

Thorax long and emaciated.

Lungs: Fibroid apices.

Heart: Normal in S. and P., no M. Tone fair, rate 80 to 90.

Pulses equal. Blood-pressure 140–90. Very little sclerotic change in radials, brachials or temporals.

Abdomen: That of the visceroptotic—space encroached upon by long thorax, flat epigastrium and bulging umbilical and iliac zones—with visible peristalsis.

Costal angle medium narrow. Visceroptotic index, 0.83.

Abdominal aorta and right iliac artery uncovered, forcibly pulsating and tender. Tender also over solar plexus and over sigmoid, the latter being distinctly spastic and contracted.

Stomach in normal position but dilated.

Transverse colon ptotic. Right kidney floating.

Rectal examination reveals only internal hemorrhoids and external tags.

Spinal Examination: Slight scoliosis to left and soreness over the left transverse processes of the fourth to eighth dorsal vertebræ, and pain on pressure over the left transverse process of the eleventh dorsal vertebra.

Extremities and joints negative.

Deep reflexes normal.

Special and Technical Examinations: Urinalyses show only faint traces of albumin, intermittent presence of indican and hyalin casts. No fixation of specific gravity; tendency to polyuria. No retention of chlorides or urea nitrogen.

Functional phenolsulphonephthalein test: 1st hour, 370 mils., 50 per cent. elimination; 2d hour, 160 mils., 20 per cent. elimination; 3d hour, 120 mils., trace; total, 650 mils., 70 per cent. plus elimination.

Blood. Moderate secondary anemia. White blood cells, 6300. Wassermann negative.

Gastro-intestinal examination: Summary of fractional gastric study:

Fasting stomach: No food rests; much mucus; 5 mils. F.Hcl =0; Total acid=20. Blood, 0.

Microörganisms plus, including Leptothrix buccalis. Few polys.

Fractional curve of anacidity, hypermotility and biliary regurgitation.

Mucus greatly increased. Enzymes and proenzymes present but deficient.

Wolff-Junghan's test for soluble albumin 1 to 40. Increased intestinal motility. Five grains of carmine powder given in a mixed meal appeared in stool in ten hours and was completely defecated at fifteen hours.

Duodenobiliary examination:

After mouth and stomach cleansing and disinfection, duodenal tube entered duodenal biliary zone in sixteen minutes. Much duodenal mucus; sphincter of bile duct open and bile discharging. Flow accelerated by douching with magnesium sulphate.

"A" bile diluted by small amount of magnesium sulphate. 36 mils., light yellow, clear, syrupy.

"B" bile 51 mils. dark greenish-black, molasses-like static bile with few mucopurulent floccules containing bile-stained columnar epithelium and leukocytes. Bacteria very evident.

Cultures from "B" bile: B. pyocyaneus and Staphylococcus aureus.

"C" bile light lemon yellow, thinly mucoid.

Examination of bile for pancreatic activity:

Trypsin: 1 mil. of bile digests 10 mils. of 0.1 per cent. solution of casein in fifteen minutes.

Amylopsin: 1 mil of bile digests 5 mils. of 1 per cent. solution of starch in thirty minutes.

Stool Examinations: Spastic scybalous and small calibered sausage masses pointed at one end, superficially covered with shaggy, stringy mucus, rather pale yellow color. No gross indigestion of food. Occult blood positive.

Microscopically: A few muscle fibers, with preserved connective tissue, but partially digested. No starch remnants. No neutral fat but many fatty acid crystals (split fats); slightly increased cellulose.

Bacterial smears chiefly Gram-negative.

Diagnostic Deductions: In somewhat their order of importance:

General Diagnosis:

A. Major.

1. Chronic toxemia.

(*a*) Bacterial, with first focus of infection probably in teeth and gums (oral sepsis, now clean) passed to secondary foci in stomach, gall-bladder and colon.

(*b*) Metabolic, from static biliary source; from intestinal and renal sources and from static vascular (splanchnic) circulation due to visceroptosia.

2. Visceroptosia.

3. Chronic cholecystitis (masked), of low grade of infective virulency and preceded by chronic biliary stasis.

4. Chronic mucous colitis, with spastic constipation, probably first due to vagotonia and now continued, owing to erosive areas in colon.

B. Minor.

1. Chronic interstitial nephritis—probably early and secondary.

2. Fibroid lungs—probably quiescent or healed tuberculosis.

3. Sympatheticotonia (dilated pupils, relatively high pressure, subsecretory states—dermatographia).

4. Low grade early toxic arthritis.

5. Chronic atrophic gastritis.

Conduct of treatment decided upon:

I. *General.* To improve toxemia by appropriate treatment of the

(*a*) Visceroptosia (bed-rest, elevation of foot of bed, properly selected and arranged diet to improve assimilation and weight-building, proper abdominal support).

(*b*) Mucous colitis (breaking chronic laxative habit and substituting "senna-fruit paste," which is gradually withdrawn; proper dietary; associated effect of transduodenal lavage and other topical treatment).

II. Direct treatment by physiological-biliary drainage to arrest the progress of the cholecystitis and to attack the biliary stasis,

considered to be the dominant causative factor of the migraine attacks (her most bitter chief complaint).

Method of Direct Treatment. Biweekly physiological biliary drainage, preceded by mouth disinfection, gastric lavage and disinfection, with potassium permanganate or silver nitrate.

After physiological biliary drainage and disinfection of duodenobiliary zone a transduodenal lavage is given of Ringer's salt, with 1 per cent. sodium sulphate, in amounts of 250 to 350 mils. Given very slowly by drip method.

This treatment was carried out for three or four weeks at the Methodist Hospital for the purpose of training the patient and nurse and to teach the principles of a visceroptotic rest cure.

Treatment then continued by nurse at patient's home in Easton, Pa., being given biweekly for five weeks more, then once a week.

Visceroptotic rest cure treatment continued.

High caloric diet, suited to her achylia, and digestion aided by substitution gastric digestants. Benzyl-benzoate was used for its effect on the spastic colitis. No laxative was given except a 2 per cent. senna paste, later decreased to 0.5 per cent.

The dark green-black static bile of molasses consistency was evident in each of the first three or four treatments in amounts of 75 to 120 mils., but thereafter gradually lightened in color to a golden yellow, the inflammatory cytological elements lessened and the bacterial content decreased and all biles showed improvement in gross appearance. An autogenous vaccine of B. pyocyaneus and Staphylococcus aureus was prepared and given twice weekly.

Progress of Case. Notes of December 17, 1919. Patient shows a wonderful improvement. Looks so much better; color less sallow —brown; skin less parchment-like; dark circles under eyes are practically gone. She has much more endurance, energy and strength. She has gained 15 pounds in three and a half months, from 91 to 106¾ pounds (kimona weight). Her bowels are moving once or twice daily, with one-half teaspoonful of 0.5 per cent. senna fruit paste at bedtime. The mucus has disappeared nearly completely from the stools. The wandering abdominal pains are no longer felt and the spastic type of bowel movement is no longer seen.

Best of all, from her standpoint, the headaches have from the onset of treatment been much less frequent, never severe, and for the past ten weeks she has had *none.*

How long her improvement will last or what will be the future development when treatment is finally interrupted I do not pretend to even guess.[14] I am not inclined to believe in so-called "cures"

[14] This patient returned to her home and continued self-treatment by this method three or four times a month. She was last examined in the office in July, 1920, and appeared to be remarkably improved. The appearance of the bile was nearly normal, the swarthiness of her complexion had disappeared and her endurance was much greater. She had maintained her gain of 15 pounds in weight, she had had no severe headaches and her bowels are moving twice daily, with no other laxative than senna fruit paste once a day.

of essentially chronic disease. Arrest of symptoms, quiescence of lesions, yes; but "cures" in the true sense I do not believe in.

I cannot close this communication without giving my hearty and sincere thanks to my associate worker, Dr. Henry J. Bartle, who has made many practical suggestions, and to Drs. Russell Richardson, S. W. Sappington, John A. Kolmer and H. B. Anderson, respectively pathologists to the Methodist, Hahnemann, Polyclinic and Pennsylvania Hospitals, for their painstaking bacteriologic work on specimens of bile submitted to them.

GLUCOSE AS AN ADJUNCT MEASURE IN THE THERAPY OF PNEUMONIA.

By Henry J. John, M.D.,

CLEVELAND, OHIO,
LATE CAPTAIN, M.C.; ASSISTANT CHIEF, MEDICAL SERVICE, U.S.A. BASE HOSPITAL, FORT SAM HOUSTON, TEXAS.

When the epidemic of pneumonia which followed influenza in 1918–19 struck the army camps we were dealing with 98.2 per cent. of pneumonias at the U. S. Army Base Hospital, Fort Sam Houston, Texas, for which we had no specific therapy. In a series of 819 cases which developed during this season the available data on sputum examinations indicate that we had the small percentage of 1.8 per cent. of pneumococcus type I variety, for which alone antipneumococcic serum type I is available. These data are not complete, due to the fact that in the extreme rush it was impossible to get complete bacteriological reports on all cases; however, they bring forth a true picture of that which is available for reference. In my series of 137 cases reported the incidence of pneumococcus type I was 2.4 per cent., thus still having 97.6 per cent. of cases for which there was no specific therapy.

Such a problem as this naturally raises the question, What is best to do under the circumstances? There being no specific therapy, can we do something in a non-specific way, and what?

In this search for something, something which might help the human organism overwhelmed with infection, I began to use aqueous solution of glucose intravenously. Some other camps had begun to use it; there was a favorable impression as to its efficacy, which seemed justifiable for the procedure. There was practically no literature available on its use in pneumonia.

Naturally there were many questions that arose in my mind at that time, for it was like starting a new experiment in a laboratory, questions which I jotted down at that time in my note-book, for I was going to try to find explanations for these, and answer

questions which I can well bring out even now, for no doubt those very questions will arise in anyone's mind who makes an attempt to use glucose therapeutically with an intelligent conception as to its effects. The questions were these:

1. What concentration of glucose should be used?
2. Should it be made up with distilled water or with normal saline?
3. What intervals should be used for its administration?
4. What is the real indication for its use?
5. Is the elimination better in these cases as compared with those who do not get glucose?
6. Does it produce a fall of temperature?
7. Has it any specific effect on osmosis of the lung tissues due to its hypertonicity?
8. Is there any lysis of red blood corpuscles? Can this be demonstrated either by direct smears from blood, by separating the plasma or by the presence of hemoglobinuria?
9. What quantity of glucose should be used at each dose?
10. What are the chills which at times accompany the intravenous administration of glucose due to, and how can they be prevented?
11. What is the explanation of the slowing of the pulse-rate and the improvement of its volume?
12. Why is the patient more comfortable immediately following its intravenous administration?
13. Is there any rise or a fall of blood-pressure?
14. How rapidly can it be given and how slowly should it be given?
15. Does the administration of glucose change the clotting time of blood?
16. Does it stimulate leukocytosis?
17. How much of the glucose is used for bodily nutrition?
18. Why is it advantageous over normal saline?
19. Is extravasation of glucose into tissues at the point of administration alarming?

These then were some of the questions that arose in my mind at the beginning and during the time that I used glucose therapy. For many of these I was able to find an explanation, for others, due to lack of time and inaccessibility to substantial research, I was not. However, I shall take up each one of these questions and present my findings, my attempts toward solving them and give them to you as I solved them.

1 and 2. I found that different concentrations, ranging from 4 to 40 per cent., had been used. The answer then was rather a vague one, and to solve it I set up two series of tubes in the laboratory, one series of glucose, ranging from 1 to 20 per cent., made up in distilled water the other made up in normal saline. To these I added a suspension of human red blood corpuscles and placed them in the

incubator for one hour at 37.5° C., then on ice over-night, making the final reading in the morning. The resut was as follows:

In the distilled water 1 to 5 per cent. hemolysis was present. In the distilled water 5 per cent. and above no hemolysis.

In the normal saline no hemolysis in any concentration. This proved one point to me: as long as I would keep above 5 per cent. solution I was safe so far as the question of hemolysis was concerned, and in the normal saline any concentration could be used.

I compromised on a 10 per cent. solution. 250 c.c. of this, for this was the quantity I used routinely, figured 100 calories, the solution being not thick but convenient for administration. In cases in which the disease was protracted where the question of nutrition came up I used 30 per cent. solution in an attempt to increase the carbohydrate intake to 300 calories per dose.

Erlanger and Woodyatt, in their experimental work, found that one can inject 0.8 to 0.9 gram per kg. body weight per hour for several hours without producing glucosuria. Thus for a man weighing 50 kg. one could inject 50 times 0.9 time 24 = 1080 grams or 1.08 kg. or over 2 pounds of sugar per day without producing glucosuria. In fact, Woodyatt cites a case in which he has been able to supply 6000 calories per day without producing glucosuria.

This point was a very interesting one to me, for it brought forth a proof that at a moderate administration there was no danger of the glucose passing through the renal filter, thus making one's work a blind issue.

3. In regard to the interval between the administrations I found that more than two doses per day were rarely necessary. In acute cases with high fever and prostration one administration in the morning, after the patient has had his bath and has been fixed up, and one after supper, when he is ready to retire for the night, were all that was found necessary. Following the administration the patient would always fall asleep and have a good rest; he would perspire, following which his temperature would drop 1 to 3°. The rest in itself was a great factor, for to a human machine that is whipped up above its normal capacity if you can give rest and sleep and slow the pulse, reduce the temperature, you have done as much as any conscientious physician can ever hope to do. You have saved the overhead expense which was threatening with bankruptcy. These were the five things which glucose always did for the patient:

1. It made him comfortable.
2. It produced sleep and rest.
3. It reduced the temperature.
4. It increased the elimination through kidneys and skin.
5. It slowed the heart and increased the pulse volume.

When only one dose a day was administered it was always given in the evening, for thus it invariably ensured the patient a good

night's rest, and in the morning one could see the bright countenance following a night's rest as compared with one who spent a sleepless night. His fighting chances thus undoubtedly were increased.

4. About the indication for glucose I would say any febrile condition is an indication for its use. When you have fever there you deal with a potential acidosis and a toxemia. This you can combat by the intravenous use of carbohydrates (glucose). You can reduce fever by its administration; you can make an uncomfortable patient comfortable; you help to tide him over. You can do no harm, only good.

5. As far as elimination is concerned, administration of glucose is followed by polyuria. The patient perspires profusely. Thus the two channels of elimination are both reached promptly and effectively.

6. Intravenous administration is followed by a drop of temperature of 1 to 3°. The increased perspiration with evaporation is what makes this drop in the temperature. Renal elimination may be an additional factor here as well.

7. In regard to its osmotic effect on the lung due to its hypertonicity I took up this question with Sollmann, of Western Reserve University. He says: "This is highly improbable. Experimental pulmonary edema is not prevented or influenced in the slightest degree by that factor. Atropin is also useless. The fluid is doubtless due to endothelial injury."

8. To determine whether or not there is any lysis in the blood stream I made the following experiments:

(*a*) I took blood at the beginning, during, at the end and eight hours after the administration of glucose from the same vein into which the needle was inserted (median basilic), some 20 cm. higher up toward the shoulder, making smears and placing the rest in small tubes on ice over-night. This experiment was not successful, as my controls showed lysis while the glucose specimens showed no lysis. Thus faulty technic was undoubtedly used, perhaps boiling of the syringes being at fault. The smears showed no changes of the corpuscles.

(*b*) Several series of urines were collected for one or more voidings before glucose administration, and on each subsequent voiding after the administration, each tested for occult blood, with the following results:

Name.	Specimen before glucose.	Specimen after glucose, successive voidings.	Fehling's test for sugar.
D.	–	– – – – –	–
S.	– –	– – – –	–
C.	–	– – –	–
A.	–	–	–
Lu.	–	–	–
Li.	–	–	–

– negative.

This then would show there is no hemolysis, for if present the hemoglobin would have to be eliminated through the kidneys and give a positive test in the urine.

9. The quantity used can be considerable provided the administration is slow. Even a small quantity of 200 to 300 c.c. if given rapidly may show traces of glucose in the urine, but if given slowly there is practically no limit to the quantity which can be used, for, as mentioned, Woodyatt has been able to give 6000 calories in one day. This is such an overwhelming proof that one cannot question the small quantities of 250 c.c. used here.

I have used 250 c.c., as this quantity is convenient to prepare. One can thus use 8-ounce bottles and prepare a large quantity at one time and keep them on hand, for efficiency of this work depends on preparedness.

The total volume of circulating blood in the human body is approximately 2500 c.c. Injecting into the blood stream 250 c.c. of glucose solution one adds 10 per cent. to the total volume of the circulating fluid. Elimination through the kidneys and later perspiration quickly compensates for it.

10. Chills follow at times the intravenous administration of glucose the same as any intravenous medication, even that of normal saline. Just what they are due to I do not know. Literature does not offer us any definite explanation. They come and we have to deal with them without understanding their pathological physiology.

One can never predict when a chill will come. Frequently a patient will get three to five doses of glucose without any chills, then the next dose is accompanied by a chill, then again he may be free from them for a dose or two and again each subsequent dose followed by one. Or a patient may again start out with a chill following the first dose and not have any more. There has been no regularity whatever to these.

For a while I thought I had found a solution to this question by the use of morphin sulphate, 0.008 gm., and atropin sulphate, 0.00064 gm. When I began to use it for quite a long period I met with no chills. I thought I had made a discovery which could be utilized in chills due even to other causes. But my joy was of short duration, for I began to have them even after these opiate-atropin doses. However, they were not as frequent as formerly. Thus I believe that the morphin-atropin does prevent a certain number of them. Water used for the preparation of glucose solution and perhaps the glucose itself may have something to do with these chills. I used single distilled water.

These chills, however, are not serious. I have seen so many of them, perhaps 200 to 300, in the 1000 to 1200 administrations, and I failed to see any harm come from them. I always tell the patient that if they have a chill not to fear, as it is of no consequence. There is nothing special to do for these chills when they come, except to apply blankets and hot-water bottles to the body.

11. The slowing of the heart-beat and the increase in pulse volume is one of the most striking features of glucose administration. What is it due to? In the first place to the increased volume of the circulating fluids. In the second place to adding fuel to the heart muscle. In the third place through combating acidosis, thus reducing the stimulation of the vasomotor center and the sympathetics. I am sorry that I was not able to have a polygraph to graphically show this point.

12. In my routine administration of glucose I used 250 c.c. of a 10 per cent. solution, with morphin sulphate, 0.008 gm.; atropin sulphate, 0.00064 gm.; tincture digitalis, 1 c.c.

One can say: The rest and the feeling of comfort were due to the opiate. It was not. At the beginning I used no opiate and the same comfort and sleep followed. Opiate, you remember, was used in an attempt to combat the chills and also to add additional comfort and rest. It was the glucose mainly that produced the rest and the comfort.

It was also not the tincture of digitalis which produced the slowing of the heart-beat, for digitalis does not act so quickly. Besides the same slowing and improvement in the pulse volume happened at the beginning when I used no tincture digitalis. This I used to digitalize the heart muscle in case a further use of digitalis were indicated.

It was glucose itself that produced the rest, comfort and sleep through:

(*a*) Additional volume of liquids to a febrile patient.

(*b*) By combating the incipient acidosis.

(*c*) By the increase of elimination.

(*d*) By the decrease of temperature.

(*e*) By strengthening the heart muscle directly and by the supply of carbohydrates to the tissues.

13. In regard to the rise or fall of blood-pressure the few careful readings I took showed a fall of 10 mm. Hg. immediately following its administration, the pressure coming up again to normal in forty-five to sixty minutes, as seen in the accompanying Chart I.

The removal of 5 c.c. of blood per kg. of body weight does not influence the blood-pressure (Macleod). From this I reason that if the removal of 5 c.c. of blood per kg. body weight does not influence the blood-pressure the addition of 5 c.c. of fluid per kg. body weight should also have no effect on blood-pressure. Thus, taking a man weighing 50 kg. and adding 5 c.c. of fluid, 50 times 5 = 250 c.c., which one ought to be able to add to the circulation without producing any effect. My blood-pressure readings seem to bring out this point.

14. As to the rapidity of administration. Naturally one cannot use too much speed for fear of cardiac dilatation. This applies especially to weakened hearts. I take fifteen to twenty-five minutes

for the administration of the 250 c.c. glucose. Too slow a procedure is also not advisable unless the receptacle can be kept at constant temperature, which is very impracticable at a bedside and quite unnecessary. All that is necessary is to allow for the cooling of the liquid before its entrance into the vein. I have made the following observations in order to show the amount of cooling during the procedure:

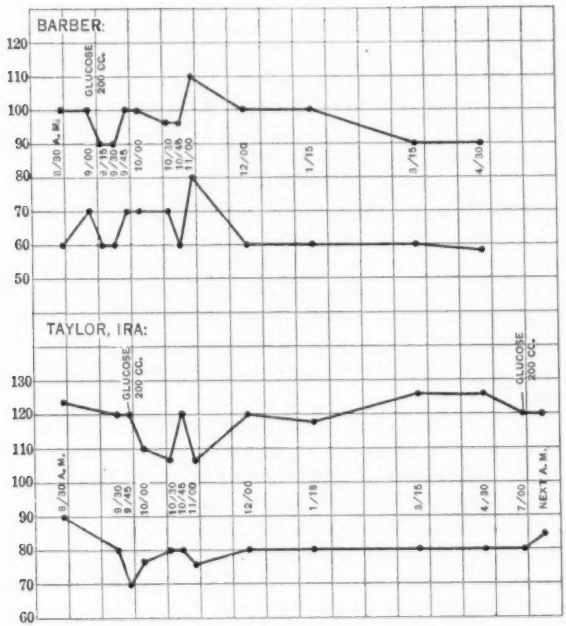

CHART I.—Observations on blood-pressure changes during intravenous administration of glucose.

A 250 c.c. bottle filled with glucose solution, a 3-way stopcock and a 10 c.c. syringe were used, the bottle being kept at a constant temperature. The exit temperature was measured from a No. 20 gauge needle in a test-tube.

Glucose, per cent.	Reservoir temperature.	Exit temperature.
10	37.5° C.	27° to 28°
10	78.0° C.	57° to 58°
30	37.5° C.	28° to 29°
30	68.0° C.	54° to 55°

From this one can see readily there is a considerable cooling of the liquid during the process of administration, so that the solution

should be considerably above the body temperature and not as usually is advocated and practised, at body temperature.

15 and 16. I have not made any determinations as to the clotting time of blood, neither that of the leukocytic stimulation.

17. All of the glucose is used for bodily nutrition. Repeated tests for sugar in the urine failed to show it in carefully collected specimens except once when a trace was found. When Woodyatt could administer 6000 calories without any production of glucosuria one naturally would not expect to find any from 100 to 300 calories.

18. In administration of normal saline one adds to the bodily fluids. This is true thus far. One does nothing more. With glucose you not only supply fluids, but you also supply food, fuel and that which you need for combating the incipient acidosis present. What does saline do to acidosis? It aggravates it (Macleod), and this is the point in question. With glucose you do all that a saline can do and a whole lot more.

19. Extravasation of glucose into the tissues is not alarming; it does no harm, the same as saline extravasation into the tissues.

I made an attempt in some cases to see what the concentration of glucose in the blood stream was just before and right after the administration of 250 c.c. of 10 per cent. glucose solution. The readings are as follows:

Name.	Date.	Before, per cent.	After, per cent.	Six hours later.
Mc.	November 27	0.130	0.190	
R.	November 28	0.146	0.269	
	November 29	0.11	0.22	0.104
P.	November 30	..	0.232	
M.	November 30	0.076	0.24	
	December 1	0.11	0.194	
S.	December 2	0.098	0.19	
W.	December 4	0.108	0.252	
P.	December 3	0.18	0.248	
P.	December 3	0.07	0.4	
	December 4	0.1	0.2	
M.	December 7	0.076	0.29	
R.	December 10	0.1	0.204	
	December 11	0.16	0.256	
	December 12	0.18	0.204	
	December 13	0.114	0.268	
B.	December 11	0.104	0.264	
	December 12	0.18	0.204	
T.	December 9	0.128	0.228	
Mc.	December 14	0.12	0.328	
	December 16	0.16	0.216	
A	December 5			
	10.30 A.M.—Sugar before glucose, 0.160 per cent			
	10.50 A.M.— " after " 0.232 "			
	11.50 A.M.— " " " 0.124 "			
	12.50 P.M.— " " " 0.152 "			
	1.50 P.M.— " " " 0.080 "			
	2.50 P.M.— " " " 0.080 "			

To show the effect on pH before and after the administration of glucose the following determinations were made on blood:

Name.	Date.	pH before.	pH after.
R.	December 13	7.6	7.5
B.	December 12	7.1	7.1
Mc.	December 14	7.6	7.3
	December 16	7.4	7.4
W.	December 31	7.5	7.4
	January 1	7.4	7.2
G.	January 1	7.6	7.4
R.	January 10	7.5	7.3

The degree of acidosis is so slight that the variation naturally is small also. However, there is a definite decrease, as the figures show.

For the physiological action of glucose and its fate in the tissues I will cite Erlanger and Woodyatt:

When a single dose of glucose is injected there is a temporary increase of sugar in the circulation. The injected sugar passes rapidly out of the blood into the tissues. During its stay in the vessels the blood volume rises and a state of hydremic plethora develops, owing, doubtless, to the binding of water by the extra glucose in the vessels. This is shown by the fall of the hemoglobin percentage and a coincident fall in the blood-sugar percentage following the initial rise. These facts have been demonstrated by Brasol and confirmed and amplified by Biedl and Kraus. Similarly during the period of absorption following the alimentary administration of glucose there is at first a rise and later a return to normal of the blood-sugar percentage, and simultaneously with the latter a fall in the hemoglobin percentage.

You can inject 0.8 to 0.9 per kg. of body weight per hour for several hours without producing glucosuria. With the injection of 0.9 or more grams per kilogram per hour glucosuria develops and the rate of sugar excretion bears a definite relation to the rate of injection. During a sustained intravenous glucose injection at the sugar tolerance rate or below it glucose passes from the blood into the tissues and there undergoes chemical polymerization, oxidation, etc., at the same rate as that of injection. There is no material accumulation of glucose in the tissues. Injections at a subtolerant rate thus have a tendency to increase the glucose content in the blood without producing any appreciable increase in glucose in the tissues. The result is a disproportionate increase of the power of the blood to hold water and a state of hydremic plethora develops and presumably persists as long as the injections are sustained. The water held by the blood must come from the tissues or from the injection site or both. If the water injected with the glucose is not sufficient to satisfy the glucose in the blood some water will flow into the blood stream from the tissues. When

the glucose injection is stopped and the last of the injected glucose passes into the tissues the water previously held by the blood is suddenly discharged into the urine. This whole phenomenon differs essentially from that obtainable with inorganic salt solutions, because such salts when injected also pass into the tissues, but when once there are not destroyed. There is therefore a possibility of salt accumulation in the tissues holding water there and in part counteracting effects of the salt in the blood stream. With sustained intravenous injections of glucose at rates higher than 0.8 to 0.9 gm. per kg. per hour the glucose utilization fails to keep pace with that of the injection and the tendency is toward some accumulation of unchanged glucose. If the kidneys are functionating actively this glucose appears on the urinary side of the renal membrane and tends to collect water in this locality, probably for the same reason that glucose in the blood produces hydremia. This tendency is expressed as polyuria. Now if the diuresis exceeds water administration, water will flow from the tissues to the blood and thence to the urine, and hydremia will be sustained as long as the water supply is adequate. But if the kidneys do not function in this way most of the unchanged fraction of glucose injected remains in the body and tends to behave like a salt, causing accumulation of water in the tissues and body spaces wherever it may go. In shock cases the secretion of urine is likely to be impaired. Accordingly the most rational application of an intravenous glucose injection in shock would appear *a priori* on theoretical grounds to consi t in long, sustained, uniform injections of subtolerant doses.

Author's Routine: 250 c.c. of a 10 per cent. aqueous solution of glucose are given b. i. d. or t. i. d. as indicated, 30 per cent. solution where there is a question of nutrition. Only chemically pure glucose should be used and distilled sterilized water. A good plan is to prepare larger quantities and use 250 c.c. (8 oz.) bottles, cotton stoppers, paraffin paper over these well down over the neck of the bottle, so that one would always have a sterile lip on the bottle to pour the solution from. Sterilize by boiling or autoclaving, then store on ice.

The method of administration is that of any arsphenamin method. Either a tube reservoir or else a 3-way stopcock with a 10 c.c. syringe can be used. In case of the latter the original bottle serves as a reservoir. The latter is more practical for private work, the first for hospital use.

Use as small a needle as you can. The smaller a needle the easier it is to enter the vein.

It is advisable to administer all the medication in glucose. I use routinely:

Tr. digitalis	1.00000 c.c.
Morphin sulph.	0.00800 gm.
Atropin sulph.	0.00064 gm.
Glucose, 10 per cent.	250.00000 c.c.

The first is to digitalize the heart muscle and the latter to secure rest and also to prevent chills which sometimes follow any intravenous medication. The solution is heated to about 50° C., and from fifteen to thirty minutes allowed for its administration.

Remember that an ounce of prevention is worth a pound of cure. Thus do not wait with the glucose administration until the patient is nearly dead and then expect any miraculous result from it.

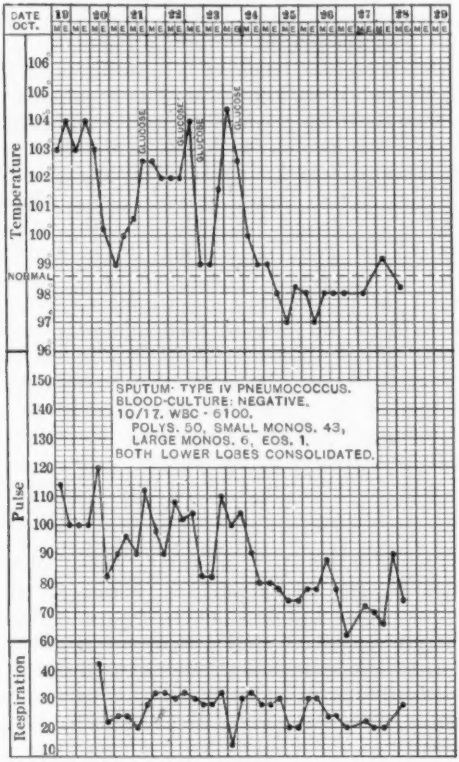

CHART II

Begin early and thus preserve the patient's strength, his natural resources, since you can do nothing specific so far as cure is concerned. Do not let the patient suffer. I think that the morphinphobia which is so impressed on the medical student has done a lot of harm when we are dealing with acute infectious diseases. The tendency is to use morphin only as a last resort, when one can see that the patient cannot live, to make his end easy. This is one of

the greatest mistakes in therapy. It should be used early, to save the patient and his natural resources, his fighting power, that he may win the victory over the infection and not be let suffer and uselessly spend his energies. It is nothing less than stupid to think that a patient will become a drug addict from the three to ten doses of morphin which he does not even know that he is getting in the glucose, but thinks that it is the glucose alone giving him the relief.

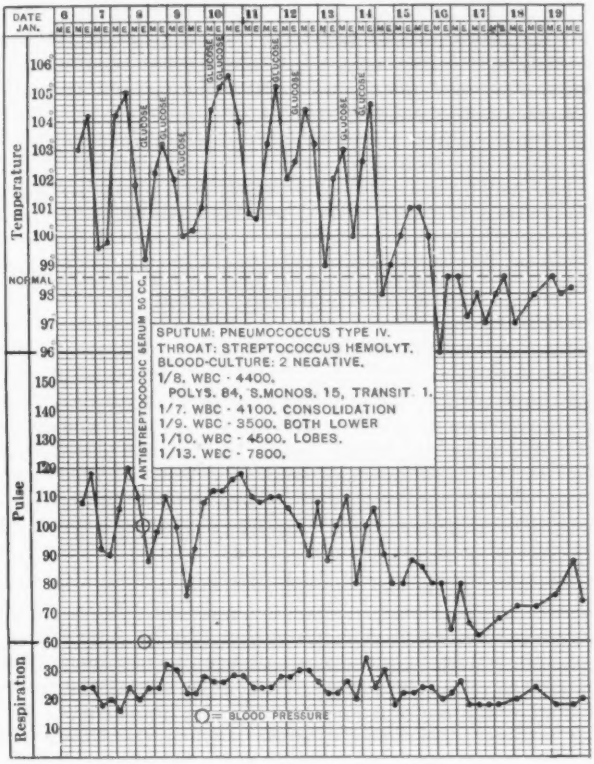

CHART III

While febrile, the patient should receive all the liquids and nourishment he will take. Fruit juices, too, are of great value.

Enemas, baths, etc., naturally should always precede the intravenous administration. After this the patient should be left perfectly quiet to rest and to sleep. A natural rest and sleep do more for the patient than all the medical armamentorium in our possession.

Our problem in pneumonia is much the same as any problem

of surgical infection. What does a surgeon do? He abides by the following principles:

1. Rest.
2. Supply of liquids and food.
3. Drainage.

Our infection is widely spread through the lung tissues, but the patient is absorbing from them just the same as the surgical case is from his area of infection. The toxic products are getting into the circulation, causing toxemia, ever, prostration and death. Through morphin and glucose you furnish rest. Through glucose you supply liquids and food to the body. The third cannot be accomplished medically. Our principle then is just the same and we can well afford to follow the surgical lead.

CONCLUSION. From the above discussion and data one can readily gather the following:

1. That the administration of glucose is without danger provided any reasonable care is used. In the 1200 administrations not a single accident developed.

2. That the patient is made comfortable and sleep is provided for him. Through this the whole organism is strengthened for the prolonged fight against the infection.

3. That the temperature is lowered.

4. That nutrition is provided for the overtaxed heart muscle without having to go through the ordinary digestive processes, storage in the liver as glycogen and reconversion into glucose again before it can be burned by the tissues. 100 to 300 calories is thus supplied to the body per each dose.

5. That a considerable amount of fluid is provided for the circulation. This together with the preceding slows the heart, producing thus artificial rest.

6. That the elimination through the kidneys and the skin is increased.

7. That practically all the medication can be supplied in the glucose, thus a much more accurate dosage can be depended on.

8. That the antipneumococcic serum type I or the antistreptococcic serum, the antitetanic serum, can be administered in this glucose medium. This is far superior to saline, for glucose will do much more than saline, thus being a much more rational medium to use as a diluent for any intravenous medication.

9. That the use of glucose is strictly a physiological measure and is to be used as such.[1]

[1] In private communication with Dr. H. O. Mosenthal, he brings out the fact that commercial glucose is preferable to the chemically pure product, which in its purification contains traces of acetic acid, and he thinks that these traces of the acetic acid have something to do with the chills that follow. His experience has been that after he had abandoned the use of the chemically pure product and resorted to commercial glucose, no chills followed. This is worth bearing in mind and publishing the results of such an investigation in the future.

A STUDY OF THE RELATIVE TOXIC EFFECTS PRODUCED BY REGIONAL RADIATION.

By W. Denis, M.D.,

and

Charles L. Martin, M.D.,

With the Assistance of Martha Aldrich.

(From the Chemical Laboratory and the X-ray Department of the Massachusetts General Hospital, Boston, Mass.)

Constant extension of the field of roentgen-ray therapy has brought into increasing prominence the condition of "treatment sickness," the constitutional reaction which frequently follows the use of massive doses of the hard roentgen rays. The underlying cause of this reaction is unknown. It has been ascribed to various and diverse factors, such as poisoning by toxic gases produced through the agency of the high-tension discharges, intoxication by protein decomposition products, by "roentgen toxins," by acid products, etc. As an excellent review of the theoretical aspect of the subject is found in the recent paper of Hall and Whipple,[1] we will not discuss this phase of the matter in detail. A factor which has, however, apparently been considered but little in investigations regarding this intoxication is one involving the question of the relative severity of symptoms following radiation of different regions of the body.

In this paper we have collected the results of a series of experiments undertaken to determine, if possible, whether by the radiation of certain portions of the body roentgen-ray intoxication is more easily produced and in more severe form than by radiation of certain other portions.

Rabbits were used in all of our experiments. Our general plan of procedure was as follows:

The animals were brought to the laboratory several days in advance, and during this period were fed on the diet (oats, celery tops and cabbage) given to all our experimentation subjects. At the end of this period 15 to 25 c.c. of blood were taken by heart punctures. This blood was used for chemical examination as described below. After being allowed to rest for from eight to twenty days, to recuperate from the loss of blood, the animals were irradiated over a single area.

A protective shield was prepared by cutting a square hole, measuring four and a half inches on a side, in the center of a large

[1] Am. Jour. Med. Sc., 1919, clxxxiv, 453.

piece of sheet lead having a thickness of approximately one-eighth of an inch. This shield could be placed over the animal board so that the square corresponded to areas 1, 2 or 3 on the rabbit, as shown in Fig. 1. The same shield was used in raying the thighs (area 4), but it was necessary to tie the animals' legs together in

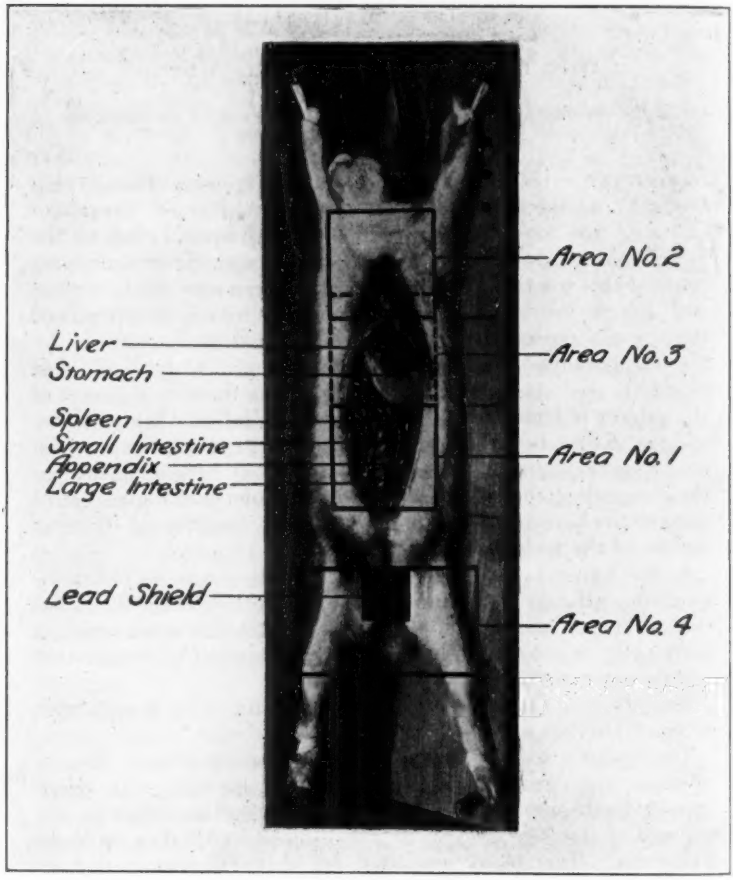

FIG. 1

order to bring them under the 4½-inch hole. Since this could not be indicated in the photograph shown in Fig. 1, a square rectangle, somewhat larger than the 4½-inch square, was drawn to show just what portions of the legs were irradiated. In raying areas number 5 and number 6, shown in Fig. 2, the same shield was used, but a

second piece of sheet lead was laid across the hole so that the irradiated areas measured 2½ x 4½ inches. All of the animal's body except the portion beneath the hole in the shield was covered with lead during irradiation. With the exception of the first dose given Rabbit No. 8, each animal received exactly the same amount of

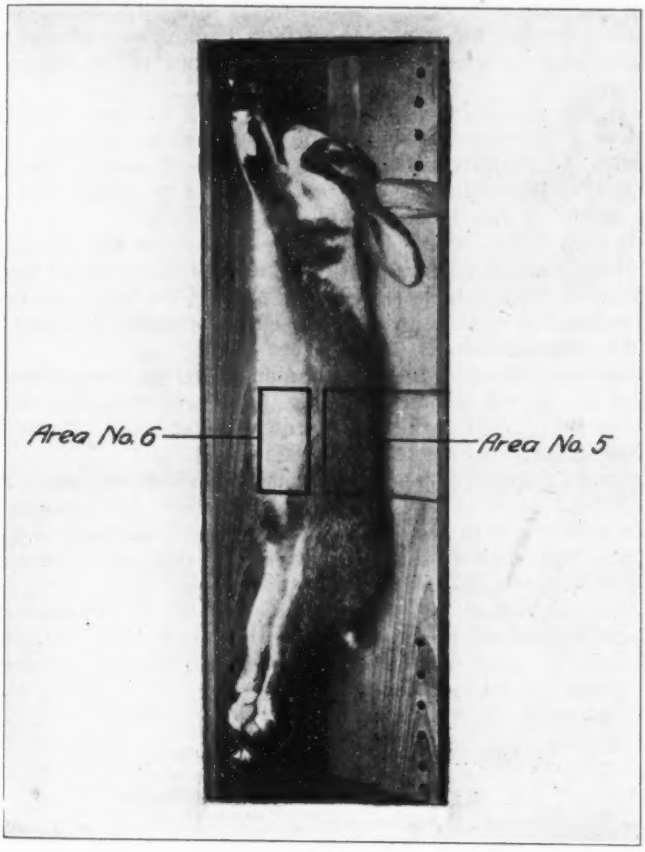

FIG. 2

irradiation as indicated by the meters measuring the electrical input to the tube. The same broad focus Coolige tube energized by the same Snook interrupterless transformer was used for all of the work. This tube was placed with the focal spot at a distance of 8 inches from the rabbit's skin and a sheet of aluminum measuring 2½ mm. in thickness was used as a filter. All of the exposures were made with the tube backing up an 8-inch parallel spark gap, actually

measured between points. When the work was first started a dose of 120 ma. minutes was administered over the abdomen of rabbit No. 8, as explained later, but apparently this dose was not sufficient to produce a toxic reaction. All of the other animals received 200 ma. minutes, and rabbit No. 8 was also given this dose when exposed the second time. It was thought advisable to break up this exposure into 5 seances, each lasting four minutes, with 10 ma. passing through the tube. About four minutes were allowed to elapse between seances to prevent overheating of the tungsten target.

For the chemical examination of the blood we have used the following procedures: For non-protein nitrogen, creatinin and creatin the methods of O. Folin and Wm. H. Folin,[2] for fat the method of Bloor,[3] and for the measurement of the alkalin reserve the technic of Van Slyke and Cullen.[4]

As from clinical experience we were led to believe that a general systemic reaction followed heavy radiation of the abdomen more frequently than in radiation of other parts of the body, our first experiments were made to study the effects produced by exposure of the lower abdomen.

Experiments Involving Irradiation of Animals over the Lower Abdomen (Area 1). As will be noted from Fig. 1, the area covered in these experiments included the large and small intestines, appendix, spleen and probably a portion of the kidneys.

Rabbit 4. Rayed over area 1, January 11; six days after exposure the animal began to show loss of appetite, a loss of weight and a decreased output of urine; on the eighth day some diarrhea was noted. The rabbit was killed on the eleventh day, as he looked so ill that we feared he would die during the night.

Autopsy. The autopsy findings were as follows: The stomach was full of food and the intestines were dilated with gas. No gross abnormalities were seen in the liver, stomach, kidneys, intestines or spleen. Histologic examination of portions of the kidney and liver showed no pathologic changes.

RESULTS ON BLOOD OF RABBIT 4 (AREA 1).

Date.	White count.	Alkaline reserve volume percentage of CO_2.	Mmg. per 100 c.c. blood.			Remarks.
			Non-protein nitrogen.	Creatinin.	Creatin.	
Jan. 4, 1920	.....	.....	51.6	1.0	4.85	
" 14, 1920	5,000	65.0	60.6	1.0	4.79	Radiated Jan. 11.
" 18, 1920	6,200	.....	65.4	1.2	4.43	
" 22, 1920	10,200	21.4	65.5	1.5		

[2] Jour. Biol. Chem., 1919, xxxviii, 81.
[3] Ibid., 1914, xvii, 377.
[4] Ibid., 1917, xxx, 289.

Rabbit 5, was rayed over area 1 on February 8. On the fourth day signs of intoxication were noted, on the twelfth day diarrhea

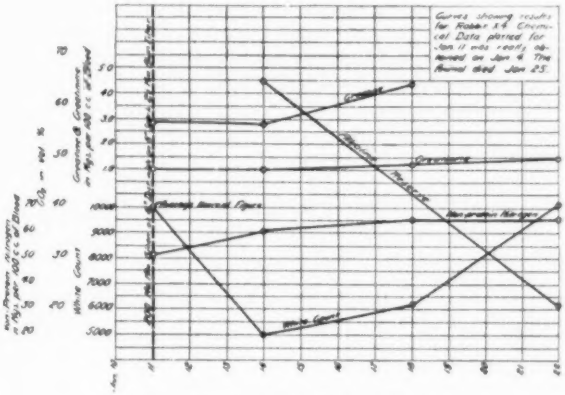

CHART I.—Results for Rabbit No. 4.

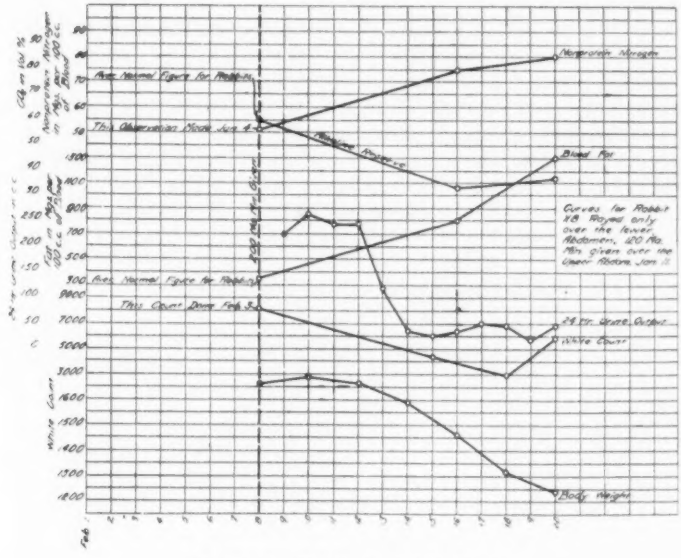

CHART II.—Results for Rabbit No. 8.

became evident and on the twenty-second day the animal was killed. The weight on the first day of the experiment was 2015 grams and on the last day 1510 grams.

An autopsy performed ten minutes after death showed the stomach full of food, the small intestine dilated with gas, the large intestine filled with liquid feces and showing a few injected areas. The kidney, liver and spleen were normal in appearance.

Histologic study of the injected areas in the large intestine revealed a complete loss of epithelium and masses of fibrin and leukocytes overlying the denuded submucosa.

RESULTS ON BLOOD OF RABBIT 5 (AREA 1).

Date.	White count.	Alkaline reserve; volume percentage of CO_2.	Non-protein nitrogen mmg. per 100 c.c. blood.	Fat, per cent.	Remarks.
Jan. 15, 1920	.....	.....	52.0		
Feb. 3, 1920	10,800				
15, 1920	4,700	.....	.....	.....	Radiated Feb. 8.
16, 1920	.....	41.8	66.5	0.53	
20, 1920	4,900	41.4	48.7	0.52	

Rabbit 7 was rayed over area 1 on February 8. Seven days later it was noted that the animal looked ill and would eat but little food; on the nineteenth day severe diarrhea set in and on the twenty-second day the rabbit was killed. The body weight on the first day of the experiment was 2078 grams; the weight just before death was 1734 grams. An autopsy performed a few minutes after death showed the stomach full of food, the small intestine normal in appearance and the large intestine and appendix much dilated and full of fluid feces. The appearance of the kidney, liver and spleen was normal. No injected areas were seen in any portion of the gastro-intestinal tract. Histologic studies of sections from the appendix and small intestine showed no variation from the normal.

RESULTS ON BLOOD OF RABBIT 7 (AREA 1).

Date.	White count.	Alkaline reserve volume percentage of CO_2.	Non-protein nitrogen mmg. per 100 c.c. blood.	Fat, per cent.	Remarks.
Jan. 4, 1920	.....	.....	55.0		
19, 1920	9800				
Feb. 15, 1920	6900	.....	.....	.....	Radiated Feb. 8th.
16, 1920	.....	39.0	58.0	0.44	
19, 1920	3000				
20, 1920	4600	46.2	51.6	0.52	

Rabbit 8 was rayed over area 1 on January 11, but only 120 ma. minutes were given. As this dose produced no apparent reaction the animal was again exposed over the same area. On February 8, on the tenth day, the usual signs of intoxication were noted; on the

fourteenth day some diarrhea appeared and on the twenty-second day the animal was killed. The body weight was 1664 grams on the first day and 1245 grams on the last day of the experiment.

An autopsy, done thirty-five minutes after death, showed the stomach full of food and much distended with gas, the small intestine dilated and the liver and kidneys normal in appearance. There were a few injected areas in the large intestine which showed a complete loss of epithelium on microscopic examination. The denuded areas of the submucosa were covered with masses of fibrin and leukocytes.

RESULTS ON BLOOD OF RABBIT 8 (AREA 1).

Date.	White count.	Alkaline reserve; volume percentage of CO_2.	Non-protein nitrogen mmg. per 100 c.c. blood.	Fat, per cent.	Remarks.
Jan. 4, 1920	.....	.....	50.3		
Feb. 3, 1920	7600	.....	.....	.....	Radiated Feb. 8.
15, 1920	4400				
16, 1920	.....	32.8	75.0	0.8	
18, 1920	3000				
20, 1920	5900	26.6	81.0	1.3	

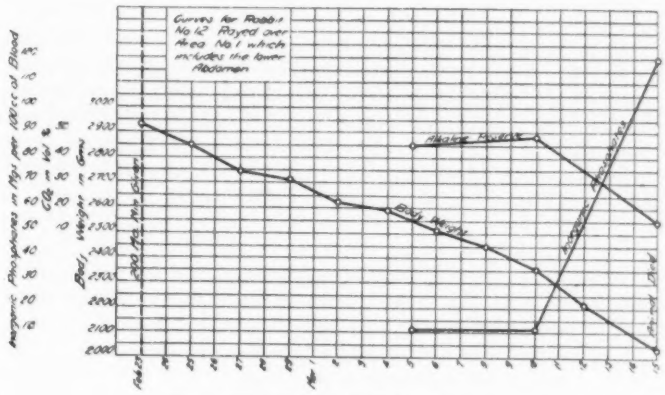
Curves for Rabbit No 12 Keyed over Area No 1 which includes the lower Abdomen
Body Weight in Grms
Leucocytes in Hundreds per c.m.m. of Blood
Alkaline Reserve
Body Weight
Leucocytes
Fat in Blood

CHART III.—Results for Rabbit No. 12.

An inspection of the results presented above indicates that in rabbits irradiation of the lower abdomen gives rise to symptoms of intoxication, accompanied by rapid loss of weight and some diarrhea. Blood examination shows a rapid fall in the number of white cells, with a subsequent approach to the initial number. In Rabbits 4 and 8 there was an unmistakable increase in the non-protein nitrogen, a fall in the alkaline reserve and in the case of Rabbit 8 a rise in blood fat. The creatinin figures were unchanged. In

Rabbits 5 and 7, however, there was no increase in the non-protein nitrogen or fat and no evidence of acidosis as judged from the standpoint of the alkaline reserve. The urine of all the animals was examined at frequent intervals, but no albumin or casts could be found, nor could we find any evidence of the presence of acetone bodies even by the use of the Scott-Wilson reagent.

On account of the blood findings indicative of some acidosis in Rabbits 4 and 8 we irradiated a fifth animal (Rabbit 12) over area 1, with the object of obtaining more data on the subject. As will be seen from the results presented below the animals soon developed the usual symptoms, and toward the end of the experiment gave evidence of great reduction in the alkaline reserve, accompanied with a marked retention of phosphates, a result of interest, in view of the findings of Marriott and Howland on the relation between phosphate retention and acidosis in some cases of nephritis.

The urine was at all times free from albumin and casts and gave no reaction for acetone.

Rabbit 12 was rayed over area 1 on February 23. Eight days later the animal developed the usual symptoms of intoxication and was killed on the twenty-third day. The weight at the beginning of the experiment was 2930 grams, at the end of the experiment 2030 grams.

March 5. Examination of the blood gave the following results: Alkaline reserve, 45 volumes per cent CO_2; inorganic phosphates of the plasma calculated as phosphorus, 3.4 mg. for 100 c.c. plasma.

March 15. Alkaline reserve, 16, inorganic phosphate of plasma, 40.0 mg., non-protein nitrogen, 232 mg. for 100 c.c.; fat, 2.6 per cent.

Experiments Involving Irradiation of Animals over the Upper Portion of the Abdomen (Area 3). This experiment was undertaken to determine whether by irradiation of the upper abdomen close to the level of the costal margin it is possible to produce an intoxication similar to that produced by raying the entire abdomen.

The area exposed included the entire thorax and the upper abdominal viscera, viz., the liver, spleen, stomach and a portion of the small intestine.

Only one animal was observed (Rabbit 16). The symptoms were identical with those occurring in the subjects used in Experiment 1, involving rapid loss of weight, diarrhea and prostration.

The weight of the animal on the first day of the experiment was 2300 and on the twenty-third day 1800 grams.

No chemical data were obtained.

Experiments Involving Irradiation of Animals Over the Chest and Neck (Area 2). As will be noted from Fig. 1 the area covered in these experiments included the heart, lungs and thyroid.

Rabbit 15 was radiated February 29. The animal continued in good condition for fifteen days, when a slight loss of weight was noted. Some days later a skin-burn, with marked contraction and loss of

hair, was noted over the radiated area. The animal was kept under observation until April 15, but up to this time showed no symptoms.

The body weight on the first day of the experiment was 2700 grams, on the last day 2720.

The following results were obtained on a sample of blood taken at the end of the experiment:

Non-protein nitrogen, 58 mg. per 100 c.c. of blood.

Alakline reserve, 47 volumes per cent. CO_2.

Rabbit 17 was rayed over area 2 on March 18. He remained in good condition until April 15, when the experiment was concluded.

The weight on the first day of the experiment was 2510 grams and on the last day 2650 grams.

The following results were obtained on a sample of blood taken at the end of the experimental period:

Non-protein nitrogen, 53 mg. per 100 c.c. of blood.

Alkaline reserve, 52 volumes per cent. CO_2.

Rabbit 24 was irradiated on March 20 over area 2 and kept under observation until April 15. During this period no symptoms suggestive of intoxication developed.

The body weight on the first day of the experiment was 2410 grams and on the last day 2398 grams.

The following results were obtained on a sample of blood taken at the end of the experimental period:

Non-protein nitrogen, 57 mg. per 100 c.c. of blood.

Alkaline reserve, 48 volumes per cent. CO_2.

Experiment Involving Irradiation over the Thighs (Area 4). This experiment was done to study the results of irradiation over an area containing no viscera. In the one animal used no reaction was obtained. After a period of three weeks a skin-burn developed, accompanied by contraction and loss of hair. Otherwise the animal appeared to be in good condition when observation was discontinued four weeks after exposure.

Experiments Involving Irradiation of Animals over the Anterior and Posterior Portions of the Abdomen (Areas 5 and 6). These experiments were carried out to determine whether there might be any difference in the toxic symptoms produced by radiating the anterior and posterior portions of the abdomen of the rabbit.

The animals were placed in the position illustrated in Fig. 2 and the standard dose applied to areas 5 and 6. The only viscera exposed in area 5 were the kidneys, although it cannot be definitely said that all of the intestines and the spleen were excluded. Only intestine was included in area 6.

Rabbit 10 was irradiated over area 5 on February 23. On the third day the animal looked ill and on the fourth day diarrhea set in. The animal was bled from the heart on the eighth, twelfth and eighteenth days. A hemorrhage resulting from the last heart puncture caused death.

Weight on the first day of the experiment was 2025 grams and on last day 1470 grams.

RESULTS ON BLOOD OF RABBIT 10.

Date.	White count.	Alkaline reserve; volume percentage of CO_2.	Non-protein nitrogen mmg. per 100 c.c. blood.	Fat, per cent.	Remarks.
Feb. 18, 1920	10,600	.....	.....	.....	Radiated over area 5.
Feb. 28, 1920	8,600	.....	.....	.....	Feb. 23.
Mar. 5, 1920	5,400	41.3	44.0	0.57	
9, 1920	6,000				
10, 1920	.....	47.2	50.5	0.67	
23, 1920	.....	32.8	53.0		

Rabbit 11 was irradiated over area 6 on February 23. Here the reaction was much delayed. The animal continued well until the eighteenth day, when it began to lose weight. On the twentieth day a serious diarrhea developed and on the morning of the twenty-second day it was found dead.

Weight on the first day of the experiment was 2165 grams and on the last day 1560 grams.

RESULTS ON BLOOD OF RABBIT 11.

Date.	White count.	Alkaline reserve; volume percentage of CO_2.	Non-protein nitrogen mmg. per 100 c.c. blood.	Fat, per cent.	Remarks.
Feb. 14, 1920	9200	.....	58.0	.....	Radiated over area 6, Feb. 23.
28, 1920	9400				
Mar. 5, 1920	5600	31.8	44.0	0.5	
Mar. 10, 1920	5000	32.0	60.0	0.8	

On consideration of the findings, in which our animals showed marked loss of weight, with the accompaniment of blood changes indicative of some acidosis, it occurred to us that the objection might be made that these blood changes could be produced simply by a condition of undernutrition. It should be pointed out, however, that our animals invariably ate all the green food provided for them but refused to touch the oats which previously had been well liked, and that at autopsy their stomachs were always full. However, in order to obtain direct evidence we kept two rabbits for a period of twelve days on a daily intake of 100 grams of lettuce, no other food except water being provided. As a result of this treatment the animals lost weight, but examination of a sample of blood taken at the end of the period gave no evidence of acidosis.

Rabbit 25 was fed on a daily ration of 100 grams of lettuce for

twelve days; weight on the first day was 2960 grams and on the twelfth day 2790 grams.

Examination of the blood on the twelfth day gave the following results: Non-protein nitrogen, 48 mg.; alkaline reserve, 49 volumes per cent. CO_2; fat, 0.45 per cent.

Rabbit 26 was fed on a daily ration of 100 grams of lettuce for twelve days. Weight on the first day 2580 grams and on the twelfth day 2281 grams.

On the twelfth day examination of the blood gave the following results: Non-protein nitrogen, 51 mg.; alkaline reserve, 50 volumes per cent. CO_2; fat, 0.70 per cent.

Discussion. In considering the results of the experiments described above it will be noted that toxic reactions were produced only in the animals exposed over areas in which some portion of the intestine was included, and, furthermore, that severe intoxications were invariably produced by irradiation of these areas. Thus even the rabbit exposed over area 5, which probably contained only a small portion of intestine, developed toxic symptoms after a rather long latent period, while a particularly severe reaction followed irradiation over area 6, which contained none of the viscera other than portions of the intestinal tract. On the other hand, animals irradiated over the thighs and over the neck and chest continued in good condition and showed absolutely no symptoms, though kept under observation for a period of several weeks. Our results would appear to confirm the findings of Hall and Whipple, who state that they believe injury to the intestinal epithelium to play no small part in the systemic reactions following exposure to the roentgen rays. These investigators, who worked with dogs, describe the same small isolated areas of epithelial destruction noted by us. These patches, which could be readily identified in the gross by small injected areas in the intestinal wall, were frequently, but not invariably, found by us at autopsy; in fact, in some of the rabbits in whom the reaction was particularly severe no such abnormality could be detected. In view of the inconsistency of these anatomic lesions we feel some hesitation in attributing much importance to them; in fact, we are inclined to suggest the hypothesis that they are, perhaps, the result rather than the cause of the intoxication.

The inhalation theory of roentgen-ray intoxication advanced by Wilbert[5] in 1899 and by Pfahler[6] in 1916 is hardly consistent with our findings. If the gases produced by the high-tension discharge from the leads running to the tube were at all instrumental in producing the reactions observed the animals irradiated over the chest and over the hind legs should have shown the same symptoms as those irradiated over the abdomen, since they were all treated in the same manner and all inhaled the same gases.

[5] Philadelphia Med. Jour., 1899, iii, 1014.
[6] Am. Jour. Roent., 1916, iii, 310.

Linser and Sick[7] and Engel[8] claim that the intoxication results from "roentgen toxin" produced in the blood. All of the blood passes through the heart and pulmonary circulation; it is spread out in numerous fine capillaries in the lungs and should undoubtedly receive thorough irradiation during an exposure of the chest. If we are to accept the "roentgen-toxin" theory, irradiation of the chest should produce a reaction as quickly as irradiation of the abdomen, a postulate which has not been borne out by our results.

Linser and Helber,[9] Rosenstern[10] and Warthin[11] believe that the intoxication results from a roentgen-ray nephritis. The kidneys of some of the rabbits who had received heavy abdominal exposures were examined histologically by Dr. J. H. Wright, who reported the entire absence of lesions. Frequent urinary examinations invariably gave negative results for albumin and casts, nor could we, except in the case of one animal (Rabbit 12), obtain evidence of any retention of nitrogen, if we may judge by the figures obtained on the determination of non-protein nitrogen in the blood. Our results, therefore, do not offer evidence of the existence of a roentgen-ray nephritis but rather are in accord with the results of Hall and Whipple, who found no abnormality in the kidneys of dogs after irradiation. Much work has been done on the effect of irradiation on enzymes,[12] and especially on the enzymes of the gastro-intestinal canal.[13] In view of the fact, however, that the intoxication produced in animals progresses slowly over a period of two or three weeks, it would appear that this intoxication must be produced by an inhibition of cellular function rather than by a chemical change in the digestive juices. Most but not all of the rabbits who received heavy exposures over the intestines gave evidence of the presence of an acidosis, as shown by a fall in the alkaline reserve and a rise in the fat and in the inorganic phosphate of the blood. This condition we feel sure cannot be due to starvation, for the animals ate lettuce and celery in generous amounts up to the day of death. The fact is not without interest that these animals refused to touch oats, an acid food, but partook freely of lettuce and celery, which is rich in alkaline salts.

In view of the relatively small number of animals used, it is perhaps premature to attempt to obtain too rigid a theoretical basis for our findings; but we would call attention to the fact that acidosis based on intestinal disturbances has been observed chemically many times. Edsall,[14] in 1902, described a case of coma with acidosis which was apparently due to intestinal upset; much has been written about the occurrence of acidosis as a result of intestinal intoxication in children. The occurrence of acidosis in Asiatic cholera has been

[7] Deutsch. Arch. f. klin. Med., 1905, lxxxiii, 288.
[8] Deutsch. med. Wchnschr., 1907, xxxiii, 22.
[9] Deutsch. Arch. f. klin. Med., 1905, lxxxiii, 479.
[10] Munchen. med. Wchnschr., 1906, liii, 1063.
[11] Am. Jour. Med. Sc., 1907, cxxxiii, 736.
[12] Ztschr. f. Krebsf., 1904, ii, 171.
[13] Am. Jour. Physiol., 1914, xxxv, 224.
[14] Philadelphia Med. Jour., June 28, 1902.

described by Sellards,[15] who, however, believes this phenomenon to be the result of the nephritis which has been found so frequently in his cholera cases.

The experiments recorded above were originally undertaken in an attempt to throw some light on the obscure cause of "treatment sickness." Before attempting to apply the results of our animal experiments to a discussion of this intoxication in the human subject, the fact must be borne in mind that the dose received by each area of the rabbit's body was about five times the dose usually given any one portion of the body of a patient; where the cross-fire method is used, however, it is conceivable that an internal organ might receive as much irradiation as did the internal organs of our rabbits; but, again, consideration must be taken of the fact that the area used in our experiments was large enough to cover half of a rabbit's abdomen, but would, of course, include only a small portion of the abdomen of a man.

A further difference in clinical "treatment sickness" and in the intoxication produced in animals is the fact that in the human subject the symptoms usually appear a few hours after exposure and last but a few days, whereas in the case of rabbits absolutely no objective symptoms appear for several days after irradiation; but once started, the symptoms become progressively severe.

Our results would suggest, although they by no means prove the fact, that the severe systemic reactions encountered after irradiation of the abdomen in patients may be in part at least caused by an acidosis. Careful and extensive work with clinical material is, of course, necessary before this hypothesis can be considered seriously. Such an hypothesis does not, and in fact need not, attempt to explain the severe reaction frequently observed after irradiation of tumors of the chest and of the extremities, for in cases in which large growths are caused to rapidly shrink by exposure to the roentgen-ray it is highly probable that toxic bodies of a protein nature may be discharged into the circulation.

We wish to express our appreciation of the valuable suggestions offered by Dr. George W. Holmes and of the kind coöperation of Dr. J. H. Wright, who reported on our histologic sections.

Summary. 1. A definite massive dose of roentgen-rays administered to the body of a rabbit produces a severe systemic reaction and death only when some portion of the intestinal tract lies within the irradiated area.

2. It is possible to produce a definite acidosis (lowering of the alkaline reserve) in rabbits by administering a heavy dose of roentgen-rays over the abdomen. Such animals give no evidence of suffering from a "roentgen-ray nephritis."

3. The results suggest the hypothesis that acidosis may be a factor in "treatment sickness" following abdominal irradiation.

[15] Principles of Acidosis, 1917.
[16] Am. Jour. Roent., 1916, iii, 356.

EPIDEMIC ENCEPHALITIS: INCLUDING A REVIEW OF 115 AMERICAN CASES.

By Arthur D. Dunn, M.D.,
AND
Francis W. Heagey, M.D.
OMAHA, NEBRASKA.

(From the Department of Medicine, Creighton University.)

During the past three years, in the wake of a world-wide epidemic of respiratory disease, there have appeared an unusual number of cases presenting the symptomatology of a disseminated encephalitis. A brief study at this time of the etiology, pathology, symptomatology, prognosis and treatment as revealed by an analysis of 115 American cases, inclusive of 15 personal cases, should be of interest, for it would seem from a survey of the literature and from personal experience that epidemic encephalitis is being repeatedly misdiagnosed as poliomyelitis, botulism, brain abscess, cerebral hemorrhage, thrombosis, embolism, meningitis, acute paralysis agitans, etc., and that the data had not been at hand on which to evaluate the symptomatology of the disease.

The advent of a "new disease" naturally aroused the curiosity of students of medical history. It was soon learned that the supposed "new disease" was centuries old and had appeared repeatedly under different names, but with similar symptoms in association with previous respiratory epidemics. Crookshank[1] opens his article with an epigrammatic quotation from Bouvier,[2] written in 1837, which is worth repeating, and which summarizes, in an inimitable manner, the results of Crookshank's investigations into the history of the disease: "On l'a dit justement, les mêmes questions renaissent à chaque épidemie catarrhale et leurs solutions diverses se réproduissent chaque fois a peu près les mêmes." Different names have been applied in the past as in the present, but the symptoms were much the same. The first cases in the present epidemic were described by von Economo[3] in Austria in 1917; by Netter[4] in Paris in 1918; by Wilson[5] and others in England in 1918; by Tilney[6] and Riley in New York, and Bassoe[7] in Chicago, early in 1919.

[1] Boston Med. and Surg. Jour., 1919, clxxxii, 34.
[2] Ann. d'hyg. pub. et de méd. Legale, 1837.
[3] Wien. klin. Wchnschr., 1917, xxx, 581.
[4] Bulletin de l'académie de médicine, Paris, May, 1918, and November, 1918.
[5] London Lancet, 1918, ii, 91.
[6] Neurological Bulletin, 1919, vol. ii.
[7] Jour. Am. Med. Assn., 1919, lxxii, 971.

Etiology.—The cause of the disease is unknown and the opinions of those who have attempted etiological investigations are at variance. In 1917 von Wiesner[8] claimed to have produced a hemorrhagic encephalitis by inoculating into the brains of apes a diplococcus obtained from one of von Economo's cases, but without reproducing the histological pictures found in man. Marinesco[9] and McIntosh saw in and isolated from the meninges and pons two types of organisms, namely, a thick, Gram-positive, anaërobic bacillus which was pathogenic for mice and a diplococcus which was occasionally associated with the bacillus. Strauss,[10] at the Rockefeller Institute, reproduced the disease in apes with filtered nasopharyngeal secretions and maintained that the cause was a filtrable virus. May we not here again be up against the same *impasse* that has prevailed in poliomyelitis: the Flexner filtrable virus—globoid bodies—on the one hand and the Rosenow streptococcus with the "globoid bodies" considered merely as variants of a streptococcus, on the other hand?

One of us isolated a green streptococcus from the blood of a case (No. 12, Tables II and III) which was recovering from influenza with bronchopneumonia, and which was at the time developing a typical epidemic encephalitis with lethargy and diplopia. The organism was agglutinated by the patient's serum only and was not agglutinated by other sera. The patient's serum did not agglutinate laboratory strains of diplococci and streptococci. The organism had the cultural characteristics of the organism which was frequently isolated from the blood and lungs in the epidemic of influenza in Omaha in 1918 (Dunn[11]). The organism died out before animal experiments could be instituted and repeated cultures later failed to recover the organism. The immediate bearing of influenza on epidemic encephalitis is a moot question. In the 115 cases here analyzed 36 gave a history of a respiratory infection within one year (average time two months) prior to the onset of the encephalitis. The relative infrequency of encephalitis in a pandemic of influenza is noteworthy. On the contrary the appearance of encephalitic disease chiefly at the periods of a world-wide respiratory infection is suggestive. Draper[12] seemed inclined to assume that a close relationship exists between epidemic encephalitis and poliomyelitis, the former being a possible variant of the latter. It is to be noted that in 12 of our personal cases 5 gave a history of repeated severe tonsil infections; of the other infectious diseases, 2 had had typhoid, 2 diphtheria, 2 inflammatory rheu-

[8] Klin. Wchnschr., 1917, xxx, 933.

[9] L. G. B., London, 1918, p. 121.

[10] Jour. Am. Med. Assn., lxxii, 20, 1493; New York Med. Jour., 1919, cix, 772.

[11] Observations on an Epidemic of Bronchopneumonia in Omaha, Jour. Am. Med. Assn., December 28, 1918, p. 2128.

[12] L. G. B., London, 1918, No. 121, p. 62.

matism, 1 scarlet fever, 1 chorea, 1 pleurisy, 1 tuberculosis of the knee.

Symptomatology. The symptomatology of epidemic encephalitis is protean. When one considers that it is the brain-stem—the great switchyard of the central nervous system—which is the site of predilection of the virus the multiplicity of symptom complexes is explained. Even microscopic lesions in such an area as the mesencephalon may be fraught with much symptomatic import. All parts of the brain-stem and cerebrum, however, are open to attack. We have found it useful from a clinical standpoint to arrange the more or less characteristic symptoms in groups or types: (1) Polioencephalitic; (2) lethargic; (3) Parkinsonian; (4) cataleptic; (5) meningitic; (6) cerebral; (7) polyneuritic; (8) myelitic. We have endeavored to place these groups on a pathological and anatomical basis. We confess that the grouping is artificial, and that, on account of the multiplicity and disseminated character of the lesions it cannot be a hard and fast one, but in the study and recognition of cases we have found it helpful. The classification has been arranged from an analysis of the symptoms of 115 cases, with acknowledgment to MacNalty,[13] Tilney and Riley (*loc. cit.*) and others. The syndromes always overlap, so that a case may easily find itself in two or more groups. For example, J. C. (Case No. 9, Tables II and III) could have been placed at different times in either of two groups: In the cerebral group on account of Jacksonian epilepsy, motor aphasia and right-sided spasticity; in the agitans group on account of tremor, spasticity and the Parkinsonian mask. Careful correlation of symptom groupings with subsequent pathological study may throw some light on cerebral localization and on the function of the "dark" areas of the central nervous system. Five of the 15 personal cases were classified as polioencephalitic (1 superior); 3 lethargic; 1 Parkinsonian; 1 meningitic; 4 cerebral (2 convulsive, 1 psychotic, 1 epileptomaniacal), 1 polyneuritic. It must be emphasized that the group to which a given case is assigned depends greatly on the time in the course of the disease at which the patient is grouped. At one period a case may fall clearly into the polioencephalitic at a later period into the lethargic group. We have excluded a poliomyelitic group, for neither in our own cases nor in the literature do we find any cases which are sufficiently frank to be called poliomyelitic. Tilney and Riley's (*loc. cit.*) case is exceptional. The lethargy in this case would not seem typical, and one case is not sufficient grounds for a separate type without pathological corroboration. We feel that the posterior poliomyelitic type can quite well be classified, temporarily at least, as polyneuritic.

[13] L. G. B., London, 1918, No. 121.

TABLE I.—SYMPTOMATOLOGY. CLASSED ANATOMICALLY.

Type.	Symptom.	100 cases.	15 cases.	Part.
Polioencephalitic Ophthalmoparetic	Cranial nerve palsies:	..	..	Midbrain, pons and medulla.
	III	60	6	
	IV	2(?)	0	
	V	7	3	
	VI	34	6	
	VII	12	5	
	VIII	4	2	
	IX	2	0	
	X	1	0	
	XI	0	0	
	XII	11	2	
	Eyes:			
	Diplopia	50	8	
	Anisocoria	25	4	
	Ptosis	20	6	
	Lack of light and accommodation reflex	12	4	
	Sluggish pupils	20	4	
	Retinal changes	10	2	
	Swallowing	13	0	
	Vomiting	8	1	
	Polypnea	1	2	
Lethargy	Lethargy	69	10	Pituitary, thalamus, iter and cerebrum.
	Insomnia	16	4	
Cataleptic	Catalepsy	20	6	Cerebellum.
	Vertigo	19	5	
	Nystagmus	17	1	
	Ataxia	4	2	
Meningeal	Headache	47	10	Meninges.
	Rigidity neck	12	1	
	Delirium	24	6	
	Kernig	3	3	
	Tache	1	0	
Paralysis agitans	Parkinsonian mask	9	3	Lenticular nucleus.
	Spasticity	..	4	
	Festination	3	0	
	Tremor	30	5	
Mycelitic	Bladder	15	4	Cord
	Reflexes disturbed	25	7	
	Babinski	14	7	
	Reflexes absent	2	2	
	Clonus	5	4	
Epileptomaniacal	Convulsions	0	2	Cerebrum.
	Paralyses	0	1	
	Asynergies	20	0	
	Epileptiform attacks	..	3	
Psychotic	Hallucinations	..	3	Cerebrum.
	Illusions	..	3	
	Depression	9		
	Delirium	24	7	
Polyneuritic	Pain in extremities	23	3	
	Sensation disturbed	..	1	
	Paresthesias	6	3	
	General symptoms:			
	Epistaxis	1	1	
	Cervical adenitis	..	2	
	Tachycardia	..	1	
	Weight loss	..	5	
	Appetite increased	..	6	
	Fever	43	13	
	Perspiration	6	15	
	Hiccough	5	0	
	Tears	4	0	

Table I has been made to show the relative frequency of individual symptoms and their grouping. This table is instructive from the symptom incidence as well as from the localization standpoint. The anatomical localization of symptoms in some instances is far from settled. Lethargy is attributed to pituitary involvement by Cushing[14] and Climenko[15] and to the thalamus by von Economo (*loc. cit.*), MacNalty (*loc. cit.*) and Flexner.[16] We have assigned catalepsy to the cerebellum because it is a manifestation of disturbance in that extrapyramidal muscle tonus controlling apparatus of which the cerebellum forms an important part. Vertigo, nystagmus and ataxia are grouped under the cerebellum also because they arise as frequently in cerebellar as in disturbances elsewhere. Disturbed bladder and deep and superficial reflexes are attributed to the cord because they occur in cord diseases, but with full realization that some of them occur quite as frequently from lesions elsewhere. The groups or types, as shown in Table I, are useful merely in calling attention to symptom-complexes and in facilitating their recognition.

Special Symptoms. Certain of the more prominent symptoms should receive comment. The incidence of what we consider the less important symptoms can be seen by consulting Table I.

Ocular Disturbances. Disturbance in the third and sixth nerves is far and away the most common symptom occurring in epidemic encephalitis. In the 115 cases third nerve palsies were present in 63 cases and sixth nerve in 39. Diplopia was the initial symptom in 19 cases and was recorded in 55 cases. Ptosis was present 21 times. Diplopia is often an evanescent and baffling symptom, for although the patient may maintain that he sees double, yet the oculist cannot demonstrate the muscles involved. We believe that this symptom is more common than the statistics would indicate, because invariably in our own cases, when the question was brought up squarely to the patient or to the relatives the presence of visual disturbances was substantiated. The absence of the fourth nerve involvement is striking in spite of the close anatomical proximity of its nucleus to that of the third. Is this due to its short and protected course on the dorsum of the brainstem? *In what may be considered as a diagnostic triad of the disease viz.*, (1) *ocular symptoms*, (2) *lethargy and* (3) *a negative or typically atypical spinal fluid, ocular symptoms hold first place.*

Other Cranial Nerves. The sensory portion of the fifth was involved 9 times in 115 cases. Apparently the motor portion of the fifth is rarely involved, and may not this be explained, in some instances at least, by its long mesencephalic sensory root which extends along the floor of the iter in close proximity to the nuclei of the third

[14] Diseases of the Pituitary, Philadelphia, 1912, pp. 101–102.
[15] New York Med. Jour., March 27, 1920.
[16] Jour. Am. Med. Assn., March 27, 1918.

nerve which are so commonly involved? In one of our cases the onset was associated with pain on the right side of the head and face, which soon shifted to the left side, and which was so severe that morphin was required. The patient did not sleep for seven days. Later a seventh nerve paralysis developed. As the pain subsided lethargy appeared. The development of a corneal ulcer on the left side, a left peripheral seventh paralysis, an involvement of the left chorda tympani and a left nerve deafness in this case are noteworthy. In the presence of the above symptoms, and with a spinal fluid showing 24 cells per cubic millimeter, globulin plus 2, a mild paretic gold chloride curve, negative cultures and smears and a negative Wassermann in both spinal fluid and blood, a *localized meningitis of unknown etiology* was assumed until lethargy appeared. This case would be explained by the meningoradiculitis conception recently advanced by Bassoe.[17] Fifteen of the cases had paralysis of the seventh nerve. The paralysis was generally peripheral in type and unilateral. The tendency of seventh nerve paralysis is to clear up slowly, requiring from four to five months. Involvements of the other cranial nerves (first, second, ninth, tenth, eleventh and twelfth) seems of minor diagnostic significance (13 cases out of 115). (See Table I.)

Polypnea occurred in 3 cases, 2 of them in our own series. In one of our cases (No. 5) a respiratory state of 60, which seemed to be of respiratory center origin, was maintained for thirty-six hours. The respirations in the other case (No. 10) were 80 to 100 per minute; they suggested irregular diaphragmatic and abdominal spasms (myoclonus) and occurred in attacks which were associated with extreme suffering, necessitating the use of morphin. This symptom, although rare, merits special attention, because when present it dominates the clinical picture.

Lethargy occurred in 79 cases and was the first symptom noted in 34 cases. It was preceded by insomnia in 4 cases. The degree of lethargy was variable. In extreme cases it may approximate a coma vigil. Usually the patients can be aroused and appear dazed as if awakening from a deep sleep. The patients, when aroused, eat and answer questions, but soon relapse into their stupor. The dazed, blank, expressionless stare is quite characteristic. The lethargy in most instances does not differ from a normal deep sleep, but on awakening a normal expression is absent. The patients are negativistic and their faces are dead. The lights of intelligence and interest are out or burn low.

Catalepsy and *catatonia* would seem to be more common than it appears from the literature, occurring in 6 out of 15 cases in our personal series and in only 20 out of the 100 cases collected from American literature. Increased muscle rigidity is common and flexibilitas cerea was noted 4 times in our 15 cases.

[17] The Delirious and Meningoradicular Type of Epidemic Encephalitis, Jour. Am. Med. Assn., April 10, 1920, lxxiv, 1009.

TABLE II.—GENERAL SYMPTOMS IN EPIDEMIC ENCEPHALITIS.

Sex, age, name, date.	General.	Medulla.	Cerebrum, iter.	Cerebellum.	Meninges.	Lenticular nucleus.	Cord periphery.
1.—U. H. (M.), 53 years Feb. 3, 1920	Weight loss; fever; perspire; chilly	...	Apathy; insomnia	Nystagmus vertigo	Headache	Mask.	
2.—F. P. K. (M.), 40 years Feb. 4, 1920	Weight loss; nosebleed; fever	...	Drowsy; insomnia	...	Headache	...	Oppenheim left; Gordon left.
3.—F. S. B. (M.), 56 years Jan. 8, 1920	Weight loss	...	.....	Vertigo	Headache	...	Knee-jerks, plus 3; Romberg.
4.—M. H. (F.), 20 years Jan. 23, 1920	Temperature 100°; cervical nodes enlarged	...	Insomnia; nervous delirium	...	Headache; photophobia; Kernig	...	Oppenheim; sphincter loss; numbness in hands; chest; clonus; knee-jerks.
5.—O. S. H. (M.), 50 years Feb. 27, 1920	Grippe, 101°	...	Lethargy; delirium	...	....	...	Pain in right arm.
6.—J. D. (M.), 50 years Oct. 19, 1919	.....	Polypnea	Coma; delirium; lethargy; clonus arms	Nystagmus; vertigo	Headache	...	Twitching arms; abdominal clonus; Oppenheim right.
7.—J. S. (F.), 5 years May 23, 1919	Chilly; fever; adenitis; scaling hands; nausea; perspiration	...	Convulsions; Jacksonian epilepsy; coma	...	Headache; photophobia irritable	...	Twitching; Oppenheim; Babinski; knee-jerks.
8.—H. H. (M.), 44 years Apr. 3, 1919	Perspiration; fever; carphologia; appetite increased	...	Lethargy; delirium; sensation?	Catalepsy	Headache; rigid neck	Tremor; mask; spastic	Babinski.
9.—J. C. (M.), 55 years Aug. 20, 1919	Dyspnea; aphonia; perspiration	...	Right-hand spasm; lethargy; motor aphasia; Jacksonian epilepsy	Vertigo; ataxia; catalepsy	Headache	Scanning speech; mask; spastic	Babinski in right; ankle-clonus; right arm reflex, plus 2.
10.—H. W. (M.), 46 years Feb. 17, 1920	Fever	Polypnea	Delirium; hallucinations; illusions	...	Headache; Kernig	...	Pain in legs; Oppenheim; incontinence; Babinski in right; knee-jerks and ankle-jerks.
11.—E. L. C. (M.), 18 years Jan. 27, 1920	Perspiration; appetite increased	...	Illusions; lethargy; insomnia; loss of memory	Catalepsy	Photophobia	...	Oppenheim; Babinski; Gordon; clonus.
12.—Mrs. B. (F.), 45 years Feb. 2, 1920	Tachycardia; nephritis; influenza	...	Illusions; delirium; lethargy; hallucinations	Catalepsy	Kernig	Spastic	Babinski.
13.—M. M. (M.), 34 years Apr. 1, 1919	Chills; fever; carphologia	...	Lethargy; delirium	Vertigo	Photophobia; headache	Tremor	Incontinence.
14.—I. F. Feb. 1, 1920	Fever; pneumonia	...	Lethargy				
15.—G. V. (M.), 25 years Jan. 25, 1920	Perspiration; fever	...	Jacksonian epilepsy	Right tremor	....	...	Babinski in right; arm-clonus in right.

TABLE III.—CRANIAL NERVE SYMPTOMS IN EPIDEMIC ENCEPHALITIS.

Name, sex, age, date.	N. II.	Nerve III.				Photophobia.	IV and V.	VI.	VII.	VIII.	IX.	X.	XI.	XII.
		Ptosis.	Diplopia	Light and accommodation.	Pupil.									
1.—U. H. (M.), 55 years Feb. 3, 1920	0	Bilateral	plus	Inability to read	Left dilated	plus	Pain; tremor in face	0	Lt.	Lt.	0	Pulse, 100	0	Lt.
2.—F. P. K. (M.), 40 years Feb. 4, 1920	Edema	0	plus	....	....	plus	0	plus rt.	0	0	0	80	0	0
3.—F. S. B. (M.), 56 years Jan. 8, 1920	0	0	plus	....	....	plus	Pain in face	plus rt.	0	Rt.	0	...	0	0
4.—M. H. (F.), 20 years Jan. 23, 1920	0	Rt.	0	....	....	plus	Pain in face	0	Rt.	0	0	90	0	0
5.—O. S. H. (M.), 50 years Feb. 27, 1920	Edema left	0	plus	....	....	0	0	plus lt.	0	0	0	76	0	0
6.—J. D. (M.), 50 years Oct. 19, 1919	0	Rt.	plus	Absent	....	0	0	plus rt.	Rt.	0	0	90	0	Lt.
7.—J. S. (F.), 5 years May 23, 1919	0	0	0	....	Right dilated irregular	plus	0	0	0	0	0	150	0	0
8.—H. H. (M.), 44 years Apr. 3, 1919	0	0	0	....	Middilatation	plus	0	0	0	0	0	100	0	0
9.—J. C. (M.), 55 years Aug. 20, 1919	0	0	0	....	Sluggish	0	0	0	0	0	0	72	0	0
10.—H. W. (M.), 46 years Feb. 17, 1920	0	0	0	....	Middilatation	plus	0	0	0	0	0	90	0	0
11.—E. L. C. (M.), 18 years Jan. 27, 1920	0	0	0	....	Middilatation	plus	0	0	0	0	0	60	0	0
12.—Mrs. B. (F.), 45 years Feb. 2, 1920	0	0	0	....	....	0	...	0	Rt.?	0	0	...	0	0
13.—M. M. (M.), 34 years Apr. 1, 1919	0	Rt.	plus	No accommodation	....	plus	0	plus rt.	0	0	0	...	0	0
14.—I. Feb. 1, 1920	0	Rt.	plus	No accommodation	....	plus	0	plus	0	0	0	...	0	0
15.—G. V. (M.), 25 years Jan. 25, 1920	0	Lt.	plus	....	Both dilated	0	0	0	Rt.	0	0	...	0	0

Headache appeared as an initial symptom in 12 cases and was present in 54 cases. It must have been confused in many instances with sensory fifth nerve involvement. Sore scalp was a common complaint. Hyperesthesias and anesthesias have been occasionally described. Severe toxic headaches occur at the onset and rapidly disappear as lethargy supervenes, unless meningeal involvement is present. Headaches in the early stages may be due in some instances to ocular disturbances, such as diplopia, photophobia, etc.

Rigidity of the neck, if present, is not, as a rule, marked. Confusion may be easily avoided in regard to this symptom if one remembers that increased muscle tonus is commonly a part of the picture of epidemic encephalitis. If marked rigidity of the neck, with Kernig's or Brudzinski's signs, exist, meningitis is to be looked for.

Tremor was present in 35 cases. The descriptions given are usually vague and inaccurate. The tremor is most commonly coarse, often unilateral and not intentional. Tremor, or twitching of the abdominal muscles, has occasionally been reported in the literature (Reilly[18] and Bassoe, *loc. cit.*). We have seen this symptom in 2 cases. Facial twitching preceding a facial paralysis by several days was noted twice in our series.

Disturbances in reflexes are not common or uniform. Four cases in the series showed an absence of deep reflexes or a hyporeflexia, 2 of which cases were fatal. The knee-jerks were as often increased as absent. Babinski's sign was present only 18 times and usually transitory. Oppenheim's sign was present in 5 of our 15 cases. Ankle clonus was present in 8 of the 115 cases. In 31 cases some changes in reflexes were noted. It would seem that the greatest value of a change in reflexes was to exclude functional disease of the nervous system, which may be difficult at the first examination. *Peripheral pain* is a common symptom, 26 cases out of the 115. It has not received the attention that it should, for we found it in 6 out of our 15 cases. The pain is commonly described as cramplike, burning, boring, shooting, occasionally associated with paresthesia, and is of the neuritic type. We are convinced that it will be frequently found if inquired into. It is probably of meningitic, radicular or neuritic origin. If cases of present-day obscure pain, neuritic in character, are carefully investigated we feel sure that some of them will fall into the class of mild cases of epidemic encephalitis.

Perspiration. Sweating, judging from our cases, is very common, from the literature, very rare Though present in all of our cases it was reported only 6 times in the 100 cases from the literature. In 6 of our cases it took the form of night-sweats, which were a

[18] Hitherto Undescribed Signs in Diagnosis of Lethargic Encephalitis, Jour. Am. Med. Assn., 1920, lxxiv, 735.

source of anxiety to the patient or to relatives. According to Crookshank (*loc. cit.*) "the sweating sickness" which was prevalent in England in the seventeenth and eighteenth centuries is the same disease which is now prevalent as epidemic encephalitis.

Fever. The average maximum temperature was 102° F. except in lethal cases, in which a prelethal rise to 105° or 106° was common. Complete absence of fever was noted in 50 of the cases. In all events fever was usually transitory and prevailed only for short periods of the disease.

Laboratory Findings. Leukocyte counts were reported on 36 of the 100 cases. They averaged 10,200 white cells, 72 per cent. of which were polynuclears. The highest count was 22,000. Of 25 counts in our series of 15 cases the average leukocyte count was 10,200, of which 71 per cent. were polynuclears. The red counts and the hemoglobin percentages were approximately normal. The Wassermann test was uniformly negative. Blood cultures were negative except in one case of the 15 series, from which a green streptococcus, which was agglutinated by the patient's serum, was isolated. The urine examinations showed only the usual changes encountered in acute infections.

TABLE IV.—CEREBROSPINAL FLUIDS.

Name.	Day of disease.	Appearance.	Pressure.	Cells.	Globulin.	Wassermann.	Gold chloride.
11.—E. L. C.	18	Clear	plus 1	2 m.	0	0	112321000
11.—E. L. C.	38	Clear	plus 1	2 m.	0	0	
11.—E. L. C.	60	Clear	0	2 m.	0	0	122210000
10.—H. W.	30	Clear	plus 1	3	0	0	
9.—J. C.	90	Clear	0	0	0	0	
8.—H. H.	35	Clear	plus 1	16 m.	..	0	
8.—H. H.	41	Clear	plus 1	12 m.	..	0	
7.—J. S.	50	Clear	0	0	0	0	1355542000
6.—J. D.	10	Clear	plus 2	3 m.	0	0	
4.—M. H.	15	Clear	plus 1	3 m.	0	0	0122300
1.—U. H.	35	Clear	plus 2	24 m.	plus 2	0	12220000
1.—U. H.	49	Clear	plus 1	11 m.	0	0	112211000
1.—U. H.	63	Clear	plus 1	3 m.	0	0	1222110000
3.—F. S. B.	70	Clear	plus 1	13 m.	0	0	00011111000
2.—F. P. K.	70	Clear	plus 1	3	plus 1	0	1111100000
13.—M. M., S. Dak.	..	Clear	plus 1	..	plus 1	0	
14.—Iowa							
12.—Mrs. B.	21	Clear	plus 1	3	0	0	
15.—G. I.	35	Clear	plus 1	0	plus 1	0	0122211234

Spinal Fluids. This table gives the findings in nineteen spinal fluids obtained from the personal series of 15 cases (Table IV). The average day of disease on which the taps were made was the thirty-sixth. The earliest tap was made on the tenth day and the latest on the ninetieth day. The fluids were all clear and came with increased pressure in 7 instances. The average number of

cells was 9 per cubic millimeter. The highest cell count was 24. The cells were chiefly mononuclears. Globulin (Nonne-Apelt test) was increased in 4 cases. All the Wassermann tests were negative. The gold chloride was mildly luetic in 7 out of 11 examinations in which this test was made.

In Table V are 64 spinal fluid examinations collected from the 100 cases in the literature. The average number of cells in the series was 16 mononuclears per cubic millimeter. The pressure was increased in only 10 per cent. The globulin test was positive in over 50 per cent.

Pathology. In a region so difficult to examine as the brain-stem it is remarkable how definite a pathological picture has been set forth by the investigators. Marinesco, McIntosh, Tilney and Riley and Bassoe have given us the most information. In the only case in our series which came to autopsy the congestion of the frontal lobes, the patchy edematous meninges and the marked thickening of the basilar meninges were apparent in the gross. On macroscopic sections the brain-stem substance was soft and numerous punctate hemorrhages were found in the mesencephalic and thalamic areas. Microscopic sections showed marked edema of the peri-aqueductal gray matter, with small hemorrhages into the white and gray matter. The venules showed perivascular infiltration, with lymphocytes, plasma cells and mononuclears. Many of the vessels were thrombosed. Neither neuronophagia nor satellitosis were present. The chief pathological changes as shown in the literature may be summed up as follows: (1) Meningeal edema and thickening; (2) softening and congestion of both gray and white matter of the brain and pituitary gland; (3) punctate hemorrhages in mesencephalon and thalamus and basal ganglia; (4) thrombosis of small vessels; (5) perivascular infiltration of small vessels of the brain-stem; (6) edema of the mesencephalic area.

Prognosis. Out of Barker's 8 cases none died; 6 of von Economo's 11 died; 7 of Netter's 15 cases died; 2 of Wilson's 13 cases died; 5 of Tilney's 20 cases died; 31 of the 100 cases collected from the American literature died. Of our series 4 out of 15 died, 4 recovered wholly in one and a half to four months and 7 at the end of two or three months had fifth, sixth, seventh and eighth nerve disturbances; one still had pain in the arm after two months. Disturbances in cerebration and equilibrium took on the average three or four months to clear up entirely. Facial nerve palsies lasted four or five months. Asthenia, depression and dizziness persisted seven months as an average. The fatal cases generally terminated in the first few days or weeks of the disease, so that the longer the course of the case the better the chances of recovery. The four deaths in our series resulted in three, five, six and sixteen weeks respectively.

TABLE V.—CEREBROSPINAL FLUIDS, 100 CASES.

	Appearance.	Pressure.	Cells.	Globulin.	Wassermann.	Gold chloride.
1	...	...	30 m.	plus 4	0	
2	Clear	...	11 m.	plus 4	0	
3	Clear	...	133 m.	plus 4	0	Luetic curve.
4	Clear	...	30 m.	plus 1	0	
5	Clear	...	2 to 7 l.	plus 1	0	Paretic curve.
6	Clear	plus 1	48 m.	plus 3	0	
7	Clear	plus 1	6 l.	0	0	
8	Clear	...	...	...	0	
9	Clear	...	...	...	0	
10	Clear	...	0	0	0	
11	Bloody	...	23 l.	0	0	
12	Clear	...	3 l.	0	0	
13	Clear	...	7 l.	0	0	
14	Clear	...	0 l.	0	0	
15	Clear	...	0	0	0	
16	Clear	plus 2	0	0	0	
17	Clear	...	4 l.	0	0	
18	Clear	...	85 l.	0	0	
19	Clear	...	20 l.	0	0	
20	Clear	...	64 l.	0	0	
21	Clear	...	66 l.	0	0	
22	Clear	...	7 l.	0	0	
23	Clear	...	29 l.	0	0	
24	Clear	...	4 l.	plus	0	23433321100
25	Clear	...	7 l.	0	0	
26	Clear	...	9 l.	plus	0	1221110000
27	Clear	plus 1	26 l.	plus	0	0112111000
28	Clear	...	25 l.	plus	0	
29	Clear	...	...	0	0	
30	Clear	...	4 l.	plus	0	
31	Clear	...	9 l.	plus	0	0122110000
32	Clear	...	10 l.	plus	0	1222110000
33	Clear	...	5 l.	0	0	
34	Clear	plus 1	12 l.	0	0	
35	Clear	...	...	0	0	
36	Clear	plus 1	35 l.	plus 1	0	
37	Clear	...	...	...	0	
38	Clear	plus 1	...	0	0	
39	Clear	plus 1	...	plus 2	0	
40	Clear	plus 1	1 l.	0	0	
41	Clear	plus 1	25 l.	plus 2	0	
42	Clear	...	150 l.	0	0	
43	Clear	...	150 l.	0	0	
44	Clear	...	50 l.	0	0	
45	Clear	...	40 l.	0	0	
46	Clear	...	30 l.	0	0	
47	Clear	...	29 l.	0	0	
48	Clear	...	106 l.	0	0	
49	Clear	...	110 l.	0	0	
50	Clear	...	60 l.	0	0	
51	0	...	5 l.	plus 1	0	
52	Clear	...	...	0	0	
53	Clear	...	...	0	0	
54	Clear	...	...	0	0	
55	Clear	...	...	0	0	
56	Clear	...	4 l.	0	0	2343341100
57	Clear	...	9 l.	0	0	
58	Clear	plus 1	...	plus	0	
59	Clear	plus 1	60 l.	plus	0	
60	Clear	plus	26 l.	0	0	

Treatment. There is no specific treatment. Adequate nursing, absolute rest and freedom from all excitement is imperative. Hospitalization is to be advised because of better control of laboratory facilities and of the desirability of repeated lumbar puncture. Lumbar puncture was of decided benefit in 10 of our own cases. The patients were brighter, the cranial nerve palsies were improved and headache was often relieved. Opium should be used with care except in the early states, when the pain is severe. The eyes must be protected from the light and from foreign bodies in cases of corneal anesthesia and orbicularis paralyses. Large doses of urotropin have been advised, but there would seem to be little evidence in favor of its use. The fluid intake of the patient should be maintained at a high level. The skin demands attention, as bed-sores are common.

Conclusion. It was thought that a statistical tabulation of the symptoms and findings of epidemic encephalitis as revealed in the American literature might be useful, especially in the recognition of the mild or aberrant forms of the disease, which would seem more numerous than is generally appreciated. A basis for the evaluation of symptoms is necessary in a disease the diagnosis of which must be made by exclusion. Either cranial nerve involvement (especially eye muscle disturbances), with or without lethargy or lethargy alone, constitutes sufficient grounds for a diagnosis of epidemic encephalitis in the presence of an epidemic when either is supported by a normal spinal fluid or an atypical spinal fluid in which there is a slight increase in cells or in globulin, or in both, a negative Wassermann, a mild paretic or luetic gold chloride curve and negative bacteriological findings.

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A CONSIDERATION OF THE AFTER-CARE OF ARRESTED CASES OF ESSENTIAL EPILEPSY.[1]

By L. Pierce Clark, M.D.,
NEW YORK CITY.

Several years ago I reported a series of arrested or cured cases of essential epilepsies before this Society.[2] The period of arrest

[1] Read before the American Neurological Association, June, 1920.
[2] The Curability of Idiopathic Epilepsy, with a Report of Twenty-nine Cures, Arch. Int. Med., January, 1912.

extended from four to twenty years. I desire at this time to make a few practical comments upon these old cases and add a few notes upon some others, and thus give a proper estimate of the prognostic permanency of an arrest and also to emphasize the importance of a follow-up treatment in all so-called cured cases. There can be little doubt that at least half of the relapses, after apparently more or less enduring arrest, could be prevented by the continued oversight and direction of the after-life of the discharged patient. This principle would not be so difficult to follow were the patients and relatives frankly dealt with regarding the proper mental hygiene which should be employed. The physician's attitude in this respect should not be dissimilar to that assumed in handling tuberculous cases whose active disease process has been brought to an arrest. It may be remembered in my previous report of some thirty cases it was a rather remarkable fact that fully two-thirds of the number reported had a more or less bad heredity. In spite of this handicap none of these cases has relapsed. Neurologists look askance at a good prognosis in such epileptic individuals, yet here another theoretical and tragic view is killed by a fact. Further, neither the length of time the disease had been existent nor the general nature and frequency of attacks played a conspicuous role in estimating beforehand the curable from the incurable. In a review of this entire material one obvious fact, however, not heretofore taken into precise account, was that all the arrested cases did not possess a marked predisposition in makeup, and that soon after coming under a precise training treatment their disease became modifiable by hygienic methods. In none of my arrested cases, as well as those of the literature on the subject, no mere one organ disfunction could have explained the epilepsy or its arrest. The disharmony of the organism as a psychobiologic whole was the great fault, and striving to overcome these special defects while modifying the general life of the individual epileptic was really what brought about a successful arrest.

These general principles are to remedy the innate defects of the constitutional makeup of the epileptic or to so adjust his life that he may find a non-stressful adjustment proportionate to his capacity of adaptation. We are all aware that, as a rule, the epileptic as an individual is incapable of the normal stress life, and even though he ceases to have fits, his epileptic makeup may still be manifested in untranquil moods, states of extreme sensitiveness, anger, petulance and sullenness, so that these less-pronounced epileptic reactions must approximate the normal before we can entertain hopes for any permanency of an arrest of the disease. One invariably finds these slighter indications of the great disorder, which formerly loomed large in the former patient's life, before actual fits recur. These temperamental faults are often not self-generated, but may

be a stress reinvoked by the parents and relatives who, having held themselves in check and being also somewhat similarly temperamentally endowed as the patient himself, may begin to apply too quickly and severely a disciplinary life to the former epileptic patient. A severe type of stressful life is not and can never be thoroughly met. The patient makes a struggle to meet the new demands, but sooner or later succumbs. In searching for the cause one should remember that the physical and mental stress factor is most frequently not immediate to the attack but may be days or weeks precedent to the actual breakdown in seizures.

Two cases of recurrence of attacks after a free interval of years will be briefly cited to illustrate the careful oversight the more permanently arrested cases need if they are to remain free from fits. A clinical study of the cases has been previously reported.[3]

CASE I is now a boy of eighteen years, an only child, born of epileptogenic stock, whose epilepsy developed at eight years. Our patient walked at eighteen months and began talking rather late at two years. He was a crying, difficult baby. He entered public school at seven but did poorly there, being inordinately slow and inattentive, and at the end of two years he was removed on account of "anemia and nervousness." At ten he attended private school, but nervousness and attacks caused his removal.

The first epileptic attack came on after a period of prolonged mental stress in keeping up with his English classes. One morning, while hurrying to get off to catch a train, he complained of dizziness and immediately fell into a severe grand mal attack. Attacks followed this first one at fairly regular intervals of every two or three months until January, 1914, after which he had no attacks for two years. After eighteen months of training treatment, and in the absence of any seizure phenomena, it was decided to allow him to return to public school, which was done for a full-time attendance without the physician's knowledge. He went back to the full-time work with the old dislike, although he was only six months behind the grade of his age. Things would have gone fairly well, perhaps, if he had had some special tutoring or a little more consideration from the teachers, who, it must be said, are often prone to be merciless upon a backward pupil. He was still poor in English and mathematics, and although he would like to have engaged in sports after school, the extra time required for his studies gave him little opportunity. The lack of a full amount of time to play, once not cared for, now became very annoying, and it was often difficult to get him to his meals when out playing. The school work gradually grew more severe; in addition to English and mathematics, in which he stood poorly, he strove to gain a standing in geography, which would enable him to enter the final examinations. An attack finally

[3] Clinical Studies in Epilepsy, Psychiat. Bull., January, 1916–January, 1917.

occurred on December 26, 1915. The school life was again readjusted and there was another long, free interval from attacks (four years).

We have in this boy the makeup in which seizure reactions were induced by a too stressful demand at school. When he was withdrawn from this difficulty and placed in an ideal environment, with a chance to develop spontaneous interests, he became responsive and began to adapt himself fully to a proper physical and mental adolescence. But when he was again thrown into the same difficulties he broke down as he did at first. After having passed a period of four years of arrest he had an attack in December, 1919, which seemed to have been stupidly brought about by the mother's insistence that her only son go to college. To do this he once more went back into the close confinement of a preparatory school in a neighboring city, took up languages and all the studies, at which he did poorly and consequently hated. He stood the application and restraint without protest, but did his work worse and worse, his reaction time increased, he dawdled more and on being pulled up sharply the renewed tension once more broke him into frank epileptic attacks. Often it seems impossible for parents to learn the innate limits of physical and mental capacity in their epileptic children; hence the importance of keeping these arrested cases under medical supervision. This boy is now again doing nicely in an all-year-round training camp; he is no longer required to look forward to a college career, but is taking a practical concrete engineering course.

Case II is a boy of fourteen years of age whose grand mal epilpesy was in arrest for seven years. He had attacks usually in a series of two to ten, and had at least three or four status periods, in one of which he had 150 grand attacks in a single day. There was no distinct nervous disorder in the family stock, but many of the father's relatives possessed the epileptic character. Our patient was a crying, stubborn child. He attended school for three months, his first trial at five years of age. It was not only difficult for him to apply himself while there, but he was absolutely incorrigible and could not sit still in the classroom. He was very sensitive, and when reprimanded often cried himself to sleep even after the mildest chastisement. He never played any game in which he could not be the leader. While it was possible for him to endure the demands of home life with rages and tantrums, later when these had to be repressed at school he could not subordinate his crude individualistic tendencies. First he grew listless, then more irritable and finally broke into an uncontrollable temper, was punished and sent home. His first grand mal attack came on one night after a particularly exasperating day at school, but he had been steadily growing more irritable and run down for a month before. After the first attack he still continued at school, with all its steadily accumulating

annoyances, until a month later, when he had five grand mal attacks in one night; since that time he has not gone to school. He was allowed to do just as he pleased, to go and come with his father in the fishing boats as he liked. In a few weeks the attacks began to subside, but he still was very irritable; little or nothing seemed to precipitate tantrums and rages, but the latter were not so severe or prolonged. Under training treatment and directing his interests from the abstract work at school to a concrete outdoor life, he gradually became more tranquil and quiet and the attacks ceased.

We now have this boy after an arrest of seven years from his disease once more becoming epileptic. We find the mother anxiously pushing him in the ordinary abstract training at school. He has had three convulsions, the first occurring in November, 1918, the second a year later, and the third in March of this year (1920). There are days when he feels stupid and can do nothing correctly; the parents have learned to put absolutely no duties upon him on those days, either in school or at home: he complains of his head feeling bad and can hardly recall anything that might have transpired during that period, showing a state of acute exhaustion due to forced efforts at school work. In each case it was one of the "dopey" days when the convulsion occurred. These days are from two to four weeks apart, usually caused by some extra excitement or fatigue. He is now five feet ten in height and weighs 143 pounds. He attends public school, and while he is behind most children of his age, he has been promoted each year. He enjoys arithmetic the best of his studies but the past year has become more interested in reading. He is very much interested in anything of a mechanical nature, especially electricity, wireless operating and automobile repairing. During the summer he works for his father around the water and in the fish market, is on regular wages and works very well, but must be watched carefully to see that he does not overdo.

As in Case I, family pride and stupidity seem to be equally responsible here. Parents of epileptic children must learn that even though free from seizures they are capable of withstanding only a certain amount of stress. If they cannot learn this then physicians must continue medical oversight.

Our next case has been in arrest for six years without any relapses to the present time.

CASE III is that of a boy, aged nineteen years, who had petit mal attacks, which he termed "dreamy turns," at eight years of age. He was born of fairly healthy stock. He had no other physical disorder aside from the petit mal and never had any grand attacks. The petit mal occurred as frequently as twenty to thirty a day. He was going to school at the time he came under my care, a few months after the petit mal began. He got along fairly well at school and did not feel particularly fatigued, although he was restless and nervous. He was always quick and impulsive in temperament and

lively and active at play. He was not a difficult child and took discipline well, although very sensitive. The bromide administration was discontinued, he was placed on a diet and a normal living regimen was established. The dreamy turns gradually became more infrequent, until by twelve years of age they had entirely ceased. He continued his education, went to a boarding academy and made satisfactory progress. He finished his schooling at sixteen and entered an exporting firm, which position he has been in for the past three years. He experiences no sensations at all, and states he can stand all sorts of stress. He eats and sleeps well and rarely gets rushed or fatigued. He is at the present time a tall, well-proportioned youth, and is the picture of health.

In this instance it was possible by tranquillizing the home environment, teaching a mild but consistently regular discipline and the induction of the proper physical regimen to restore this patient to a state of normal health. His present work enables him to gradually increase his hours of responsibility proportionate to that which he is able and desirous of undertaking.

Case IV.—Our next case is a man of twenty-two years, whose epilepsy has been in arrest for three years. He was born of neurotic parents. At birth he showed an extraordinary supersensitiveness—he started, trembled and cried at the least excitement. His first attack occurred at five years after physical exhaustion and eating indigestible foods, since which time he has had attacks on an average of one or two each year. He learned easily, but his interest in school was so dilatory that his standing was poor. He was so supersensitive that "bad news always made him sick." It would be days before he could get over disappointments. He was very affectionate, conscientious and overprecise about everything, and has always been so from earliest childhood. Four years ago this patient spent several months at Craig Colony, where he kept actively employed, with various mechanical occupations, repairing automobiles, etc. As an illustration of maladjustment the following psychotic episode is so classic as a forerunner to epileptic attacks that this patient's statement may be given here to show his attitude toward his environment:

"Two months ago I noticed that I was getting irritable and dissatisfied. It was difficult to get used to the life here, but I tried hard. I felt suppressed on account of the restrictions, and the daily routine was so trying, but the doctor said it was the right place for me, so I made up my mind I would stay or die. Gradually the feeling became so strong I felt I must get away. I could not bear it any longer. I missed the social life—no dancing or anything. The feeling kept getting worse. If I even spoke to a girl I was reported. One evening another fellow and myself took a walk with two girls and next day I was severely reprimanded. I cannot tell you how I felt that night. I cannot recall any dreams. I thought

that if I could not even take a walk without being called down that I would go home or some place else where I would have some rights. Things kept getting worse, and I though more and more of home and began to write telling how dissatisfied I was with everything. When I get thinking about home and about writing home I always feel depressed, and I am not satisfied until the letter is written. When I had finished a letter to my mother I went to post it and had the attack on the way. I felt tired afterward and did not feel like doing anything. I had been looking forward to having a vacation, but the attack seemed to take the desire away and I began to feel I was not able, and the doctor would say it was foolish to think of going away. So the wanting to go did not seem so strong. After the attack I think I was relieved a little of the extreme irritation—for a time at least. I feel sure, however, that this attack would not have come on if I had had a vacation at the time I wanted it."

After leaving the Colony our patient worked in a garage repairing automobiles, and although he worked hard he seemed to feel quite content to do so. In the fall of 1918 he went to a training camp as a Y. M. C. A. Secretary and stayed there until August, 1919. He then took up salesmanship in a motor car company and continues in this field. He is out in the open air a great deal, is interested in his work and feels that he has entirely recovered from his epilepsy. He has been free from attacks for over three years.

One often hears the inquiry, Do epileptics themselves really gain an insight into the nature of their disorder and their innate temperament? A propos of this I may extract a paragraph from this former patient's letter:

"I always look back with gratitude to the time my eyes were really opened to the nature of my disease and the kind of individual that I am. In addition to paying proper attention to the routine of living I keep myself properly and interestingly employed. I take no sedatives or laxatives, and am in good physical trim. I know full well that my victory over my disease has been brought about by my learning about myself. I suppose I shall always have to refrain from certain stresses and things of an irritating nature."

Unfortunately not merely insight but reëducation is necessary before an epileptic individual may be permanently helped. This latter case underwent a training treatment of three years before the desired results were obtained.

CASE V.—The final case may be briefly cited of a man, now thirty-five years old, who has been free from grand mal attacks for over ten years. The grandfather and father were both epileptic. Our patient had been for ten years an epileptic, when a general training plan of treatment was undertaken. He is a college-trained agriculturalist and now owns and operates a large grain and fruit farm. He was married several years ago after a vasectomy. In the absence

of a family of his own he has adopted several children and is living a contented and happy life. He is so sure of his poise and tranquillity of mind that he contemplates having the function of the vasectomy restored, but the possibility of the transmissibility of so strong a heredity is a factor which must be given serious consideration.

We may conclude that: (1) So-called cures or arrests in essential epilepsies are brought about only by the most thorough-going and prolonged plan of neurologic and hygienic training treatment in which reëducation is the basic factor. (2) That relapses in arrested cases occur through negligence or disregard of the essential factors. There is renewed and intensive physical and mental stress and that proper and appropriate medical supervision should be continued throughout the lives of such individuals. Such a plan of after-care in private and institutional practice would greatly diminish the possibilities of relapses. (3) That a more or less enduring arrest and cure in essential epilepsy may be considered permanent when the environment and life reactions as regards the secondary epileptic reactions are approximately normal. That no mere cessation of epileptic fits under sedatives should be held out as an enduring arrest unless the individual shows a corresponding absence of epileptic reactions of all sorts.

VIRULENT DIPHTHERIA BACILLI CARRIED BY CATS.[1]

By Major James S. Simmons, M.C.,
CHIEF OF THE LABORATORY SERVICE, WALTER REED GENERAL HOSPITAL, TAKOMA PARK, D. C.

The available literature dealing with the transmission of diphtheria from cats to human beings is not convincing, due chiefly to the fact that the bacteriologic studies and reports are incomplete. However, many instances are on record which apparently show a relationship between animal and human infections, based upon clinical observations alone.

Thirty years ago Klein[2] described lesions in cats which he considered typical of natural infections with diphtheria bacilli. Low,[3] in 1888, reported the occurrence of four cases of diphtheria in one house, which he thought had been carried by a pet cat from another case in the same neighborhood. Cultures from this cat contained

[1] Published with permission of the Surgeon-General, U. S. Army, who is not responsible for any opinion expressed or conclusions reached herein.
[2] Local Government Board Report (Gr. B.), 1889, pp. 162–174.
[3] Ibid., 1888, xviii, 131.

morphologically typical diphtheria bacilli. Karlinski,[4] in 1908, published observations of an outbreak of diphtheria which resulted in the death of seventeen out of twenty-four Angora cats. He stated that typical pseudomembranous lesions were found from which he isolated virulent Klebs-Loeffler bacilli. He also reported a number of cases of diphtheria in children who were infected after contact with sick cats. In the same year Graham-Smith[5] made the following statement: "A general impression prevails that cats contract diphtheria from human subjects and very numerous instances are quoted in the literature of cats apparently suffering from diphtheria communicating it to children; and other examples are quoted of cats, although remaining quite well, being the only probable carriers of infection. Very few of these cases seem to have been bacteriologically examined, and in no instance has the presence of diphtheria bacilli been satisfactorily proved."

The following case was brought to my attention in July, 1919, by Capt. W. C. Deming, M.C., U.S.A.:

Mrs. P., an elderly lady, who lived in Maryland, had been very ill with a "severe tonsillitis" for four days, when Capt. D. was asked to see her on July 13, 1919. Examination at that time showed that the patient's uvula, both tonsils and posterior pharynx were covered with a grayish-brown false membrane. She breathed with difficulty and appeared to be very weak. Ten thousand units of diphtheria antitoxin were given immediately and cultures were made from the pseudomembrane. In spite of treatment the patient died early the following morning. The culture, which was examined at the Walter Reed General Hospital laboratory, showed a luxuriant growth of diphtheria bacilli. These organisms killed guinea-pigs in six days after subcutaneous injection, but failed to produce lesions in animals previously injected intraperitoneally with diphtheria antitoxin.

Cat A. A pet cat, which often slept in the bed with Mrs. P. and was "constantly fondled by her," had been sick one week before the patient's illness began. The cat had a "croupy cough, was unable to swallow food, became very thin and cried continually." It was thought that a piece of chicken bone had become lodged in the animal's throat. The cough persisted until July 13, after which the cat appeared to be improving, although it was still quite thin. Throat cultures on July 14 showed bacilli which were morphologically similar to those obtained from the patient. The virulence for guinea-pigs of the two cultures was also the same. Two days later the cat was chloroformed and a careful postmortem examination was made. The only lesion found was a small oval

[4] Ueber eine durch Hauskatzen Verbreitete Diphtheritis-epidemie bei Kindern Heilkunde, Berlin. u. Leipzig, 1908, p. 129.

[5] The Bacteriology of Diphtheria (Nuttall and Graham-Smith), Chapter VII, p. 281.

ulceration covered with a yellowish-gray pseudomembrane, between two smaller red inflammatory areas on the upper surface of the left nasal fossa (Fig. 1). Neither the fatty degeneration of the kidneys described by Klein nor any other lesion of the internal organs was found. Cultures made from the nasal pseudomembranous lesion contained diphtheria bacilli.

Cat B. Throat cultures made of another cat which had often played with Cat A were positive July 18 for morphologically typical diphtheria bacilli. After confinement in a cage at the laboratory

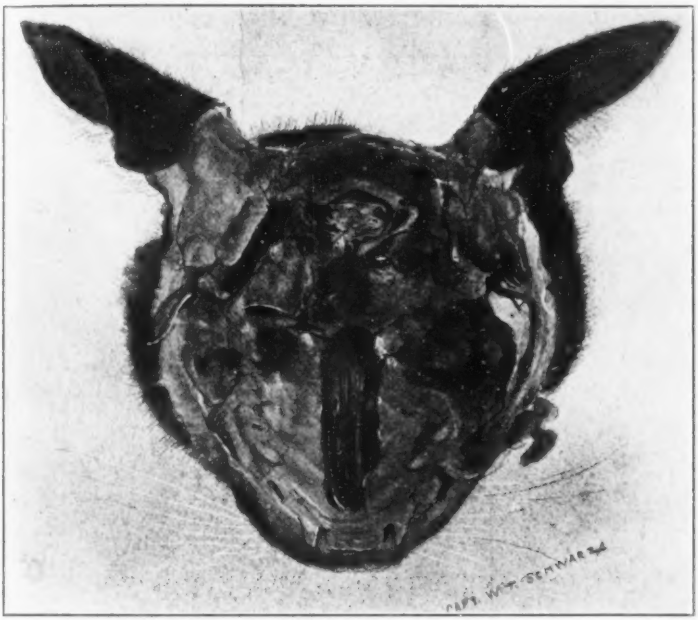

FIG. 1.—Nasal diphtheria. Cat A (specimen in Army Medical Museum, Washington, D. C.). The lower jaw has been removed and an opening made through the roof of the mouth into the nasal fossæ. Virulent diphtheria bacilli were isolated from the small oval lesion on the left.

for eight days this cat died. At necropsy small, elongated, grayish-white patches of pseudomembrane were found covering ulcerations of the vocal cords. These were surrounded by a narrow red area (Fig. 2). Diphtheria bacilli, which killed guinea-pigs in four days, were isolated from these lesions. Diphtheria antitoxin protected guinea-pigs against this organism.

Three stray cats caught on the hospital grounds and examined at this time were negative. A small, slender, granular, Gram-positive bacillus of the diphtheria group was obtained from the

throat of Cat 1. However, it differed culturally from the true diphtheria bacillus and was not virulent for guinea-pigs. None of the control cats showed any pathologic lesion.

Bacteriologic Data. The organisms isolated from lesions of cats A and B and the patient, Mrs. P., showed the following common characteristics: Colonies were grayish-white, moist, confluent and non-adhesive after growing upon Loeffler's serum media at a temperature of 37.5° C. for twenty hours. After several days' incubation they became yellowish. There was no proteolytic action in cultures six weeks old. Granular bacilli similar to Wesbrook's types C and D, which were Gram-positive, Neisser-positive and not acid-

FIG. 2.—Laryngeal diphtheria. Cat B (specimen in Army Medical Museum Washington, D. C.) shows lower jaw, upper portion of the trachea and the larynx spread open. Virulent diphtheria bacilli were isolated from ulcerations on both vocal cords.

fast predominated in smears from the younger colonies. In glucose infusion broth cultures a granular deposit was formed without clouding. Pellicle formation occurred. Small, round, moist, gray, non-hemolytic colonies were formed on horse-blood agar plates in twenty-four hours. A trace of acid without coagulation developed

in litmus milk cultures. No indol was formed. Acid without gas was formed in glucose, maltose and dextrin; alkali in mannite and inulin, while no change in reaction occurred in lactose, xylose and arabinose broth cultures. Both cat cultures produced acid in saccharose while the patient's culture became alkaline. As the ability of diphtheria bacilli to ferment saccharose is extremely variable, this difference does not prove that the three strains were unrelated. For the determination of virulence, guinea-pigs weighing 300 grams each were inoculated subcutaneously with 1.5 c.c. of seventy-two hour broth cultures, and animals were examined as soon after death as possible. A similar dose was given to control guinea-pigs previously inoculated intraperitoneally with 100 units of diphtheria antitoxin. None of these control animals died. Cultures from Mrs. P. and from Cat A both killed pigs in six days, while the Cat B culture killed a pig in four days.

Source of culture.	Granular bacilli.	Days required to kill guinea-pig.	Control guinea-pig (diphtheria antitoxin).	Typical reaction to stains.	Typical characteristics on Loeffler's media and broth.	Acid production—carbohydrate media.								
						Glucose.	Saccharose.	Maltose.	Dextrin.	Inulin.	Mannite.	Lactose.	Xylose.	Arabinose.
Cat A became ill July 2; lesion left nasal; partial recovery; chloroformed July 16	Yes	6	Lived	Yes	Yes	Yes	Yes	Yes	Yes	No	No	0	0	0
Patient, Mrs. P., became ill July 9; lesion pharyngeal; died July 13	Yes	6	Lived	Yes	Yes	Yes	No	Yes	Yes	No	No	0	0	0
Cat B became ill, date unknown; lesions of vocal cord; died July 26	Yes	4	Lived	Yes	Yes	Yes	Yes	Yes	Yes	No	No	0	0	0
Positive control (National Vaccine Co. strain)	Yes	1¼	Lived	Yes	Yes	Yes	No	Yes	Yes	No	No	0	0	0
Cat No. 1; negative control from post	Yes	Avirulent		Yes	No	Yes	No	Yes	Yes	No	No	0	0	0
Cat No. 2	No organisms of the diphtheria group found.													
Cat No. 3	No organisms of the diphtheria group found.													

Yes = acid. No = alkali. 0 = no change.

The organisms obtained from the throat culture of control Cat 1 was a small, slender, Gram-positive, non-acidfast granular bacillus. Colonies on coagulated serum media were yellowish, round, dry,

adherent and emulsified very poorly. No proteolytic action was observed. Cultures had a disagreeable odor. A cloudy growth without pellicle formation occurred in glucose infusion broth cultures. Colonies on horse-blood agar plates were gray and very minute even after forty-eight hours' growth. Litmus milk was unchanged; no indol was formed in peptone cultures. Acid was formed in glucose, maltose and dextrin; alkali in saccharose, inulin and mannite, while no reaction occurred in lactose, xylose and arabinose broth cultures. This organism was not virulent for guinea-pigs.

The history of contact and the dates of infection, when considered with the bacteriologic findings, suggest that Cat A was the source of the diphtheritic infection developed by Mrs. P. as well as that of Cat B, but this cannot be proved, However, it is certain that both of these cats were infected carriers of virulent diphtheria bacilli and therefore a menace to human beings.

Summary. 1. An elderly lady developed a fatal diphtheritic pharyngitis after close contact with a cat (A) which had been sick one week.

2. A second cat (B) which had been in contact with the first cat (A) became sick and died ten days later.

3. The patient had a grayish-brown pseudomembrane covering her uvula, tonsils and posterior pharynx. Cat A had a small yellowish-gray pseudomembranous ulceration in the left nasal passage and Cat B showed ulcerations of both vocal cords, covered with a grayish-white false membrane.

4. Diphtheria bacilli of intermediate virulence for guinea-pigs were isolated from all three lesions.

REVIEWS

PRACTICAL PHYSIOLOGY. By RUSSELL BURTON-OPITZ, M.D., PH.D., Associate Professor of Physiology, Columbia University, New York City. Pp. 238; 123 illustrations. Philadelphia and London: W. B. Saunders Company, 1920.

WITHIN a few months after the publication of his acceptable *Text-book on Physiology*, Burton-Opitz presents an equally acceptable volume on *Practical Physiology*. This manual consists of preface, fifty lessons occupying about three hours each, a list of fifty demonstrations (without directions—for use at the discretion of the demonstrator—and making a satisfactory supplement to the students' experiments), interleaves for special notes (students are expected to keep collateral note-books for verbal or kymographic records of results), tables of weights and measures with metric equivalents and complete index. Topics for experimentation cover basic subjects: First, physiology of muscle and nerve, then circulation, respiration, nervous system and sense organs, concluding with digestion, absorption and excretion. In general the apportionment is well balanced although nervous system and sense organs might well have a larger share. Illustrations are a notable feature consisting of diagrams of apparatus, arrangement of apparatus with tissue or organ, copies of kymographic records and anatomical areas. Directions are marked by conciseness and demand for only simple apparatus.

Many teachers of physiology will doubtless agree with the reviewer that this book would be of even greater value if arranged topically only; because inequality of work necessarily occurs. We hope that in his next edition Burton-Opitz will adopt this less mechanical plan.

In the preface the author explains the "inestimable value" of experimental physiology to students. "It cultivates the faculty of close observation and accurate recording of facts. It develops the power of logical thought and expression and impresses upon them facts and principles otherwise scarcely noted and comprehended. . . . It also enables the students to familiarize themselves with the use of operative instruments and the action of different drugs." Plainly, such training is the stepping stone to clinical medicine, therefore teachers and students of physiology are indebted to the

author for emphasizing this application of physiological principles which is an important line of progress today. This book deserves a place in the equipment of every physiological laboratory.

R. W. L.

HERMAN'S DIFFICULT LABOR. By CARLTON OLDFIELD, M.D. (LOND.), F.R.C.S. (ENG.); Hon. Obstetric Surgeon to the General Infirmary, Leeds; Lecturer in Gynecology, University of Leeds; Hon. Medical Officer to the Maternity Hospital, Leeds. Sixth edition, revised and enlarged. Pp. 573; 198 illustrations. New York: William Wood & Co., 1920.

THE present edition of this standard text-book on obstetrics appears under the editorship of Dr. Carlton Oldfield, who has revised and enlarged the text of the fifth edition, which appeared in 1910. As the previous editions have been extensively reviewed in this JOURNAL, an exhaustive review seems unnecessary and attention will be called only to the principal points of the revision.

The influence of the progress in surgery made during the World War is reflected in the recommendation of the use of the Carrel-Dakin treatment in cases of incomplete rupture of the uterus and septic conditions of the pelvis. The section on Cesarean section has been rewritten and its more extended use advised in certain forms of antepartum hemorrhage. The subject of transfusion for hemorrhage and shock following delivery in especially well handled. The volume closes with chapters on retrodisplacement of the pregnant uterus and eclampsia, which while not examples of difficult labor are pertinently included in a book of this nature. The remarks on arterial pressure in pregnancy and eclampsia are not in accord with the teachings of most American texts on obstetrics.

P. F. W.

THE PRINCIPLES OF ANTENATAL AND POSTNATAL CHILD PHYSIOLOGY, PURE AND APPLIED. By W. M. FELDMAN, M.B., B.S. (LOND.). Assistant Physician to and Lecturer on Child Physiology at the Infants' Hospital. Pp. 694; 129 illustrations and 6 plates. London, New York, Bombay, Calcutta and Madras: Longmans, Green & Co., 1920.

THIS rather unusual monograph aims at encompassing within a single volume a complete and detailed account of the up-to-date physiology of the various antenatal, natal and postnatal phases of child life, and the author has succeeded remarkably well in achieving his purpose. While the book is really a compilation of extracts from the literature on this subject, yet the assimilation of

the abstracts and the arrangement of the text makes the reading an easier matter than to be expected. The book will be of interest not only to the embryologist and physiologist from the aspect of the pure principles of development and organization of the fetus and child, but as well to the pediatrist and obstetrician from the practical application of these principles to the problems of the newborn and growing child. The natural discussion of the merging borders of pathologic and normal physiology of the various periods serves only to enhance the value of the book, and it should be a welcome reference volume to the classes of readers named.

The book is divided into four parts: Part I takes up the physiology of the anteconceptional and conceptional germinal stages, with an extended discussion of the laws of heredity and the post-conceptional or intra-uterine stage, the physiology of the developing child and the physiology of pregnancy. The chapters on fetal development and physiology comprise a full third of the text and form an exhaustive review of the literature of the past thirty years on this subject. Part II deals rather shortly with the physiology of birth. To the reviewer it seems that the scant paragraph on the effect of labor on the fetus might be lengthened to include a discussion of fetal asphyxia and some of the other forms of altered physiology which result in fetal death during birth. And while the spirit of criticism is present, it may be mentioned that in Part III the section on hemophilia is not fully covered at least in American literature. The postnatal stage, Part III, begins with the physiology of the neonatal period and thence progresses in an orderly manner through the various periods of infancy and childhood to puberty and adolescence, giving a history of the growth and development of the different body systems in their manifold physiologic changes. Part IV is an estimable *résumé* of the anatomic and physiologic peculiarities of the premature infant which merits more than passing attention. The text is interspersed with numerous illustrations, charts, tables and diagrams correlating the text and showing more clearly the application of the principles of physics and physical chemistry to the physiologic principles discussed. P. F. W.

RESEARCHES IN UROLOGY. COLLECTED REPRINTS FROM THE BRADY UROLOGIC INSTITUTE, Johns Hopkins University and Hospital, Baltimore. Volumes I and II, 1920.

THE reviewer was astonished, some years ago, to hear an enthusiastic novitiate in a specialty say that he had listed eighteen different problems for research investigation in his field that he felt would be interesting and productive. Doubting that any average specialist could write offhand a dozen such problems in his limited field of work, it is a real pleasure to find in these two

volumes, representing seven years' work, such a remarkable diversity of endeavor. There are 97 reprints representing 50 separate research studies, 22 articles dealing with interesting case reports and new operative procedures, and the remaining 25 are of general character, such as papers read before societies summarizing work along certain lines.

Volume I groups together papers on the kidney, the ureter and the bladder. Here will be found the collected reprints of Macht's work on the "pharmacology of the ureter," the effect of various poisons and alkaloids, leading up to the demonstration of the action of papaverin as the best inhibitor of smooth muscle spasm; Burns' work on thorium as an agent for pyelography; Geraghty on pyelitis, on bladder tumor, on primary hydronephrosis and on kidney function tests; Young on fulguration of incarcerated ureteral calculi, on his "punch" operation, on the surgical treatment of vesical diverticulæ, a valuable study on the embryology and surgery of double ureter and kidney, and a graphic description of the formation, building and operation of the Brady Institute.

Volume II groups together the papers on the prostate, the urethra and miscellaneous subjects. Again we find the pharmacological work of Macht, with the development of benzyl benzoate; White's, Davis's and Hinman's studies on urinary antiseptics, work that has produced at a later date mercurochrome; Young's researches with radium and surgery in prostatic carcinoma; Watson and Geraghty on the development and pathologic roles of the seminal vesicles; Hinman on testicular tumors; Young's new operation for epispadias and Young and Stone's operation for urethrorectal fistula.

There is no doubt that such centralization of interests is the ideal way to stimulate research. However, it is burdened at the same time with the artificial stimulus that production is essential. These volumes contain but little chaff and their greatest value lies in the grouping of allied papers otherwise scattered in the journal literature, in an appreciation of the splendid work being done for the advancement of knowledge, and in the incentive to new thoughts that their perusal gives. A word must be added to commend the excellent illustrations by Didiesch that many contain.

A. R.

MANUAL OF PEDIATRICS. FOR STUDENTS AND DOCTORS. By DR. WALTER BIRK, Professor of Pediatrics, University of Tübingen. Volume I. Fourth edition. Pp. 269; 25 illustrations. Bonn: A. Marcus & E. Weber, 1920.

THE first volume is devoted to the diseases of infancy. The first chapter gives the physiology and pathology of nursing, and

is shorter than similar portions of American texts, but it furnishes the information in a concise form. The second chapter presents the physiology and pathology of the newborn in a brief but sufficiently detailed manner The third chapter deals with the nutritional disturbances of infancy and their treatment. This forms the larger part of the volume and is excellent in the manner of presentation and in the information given. No space is devoted to the various methods of working out percentage formulæ When mixtures are recommended they are given in terms of fractional quantities of the ingredients, as, for example, one-third whole milk and two-thirds barley water. A broader consideration of methods of infant-feeding in addition to the author's own would have greatly enhanced the value of the book as a work of reference. The final chapter outlines the other diseases of infancy The chronic infections, such as tuberculosis and syphilis, diseases of the urinary, cardiac, respiratory and nervous systems are covered in a very sketchy manner. Here also the value of the book for reference purposes is greatly diminished by the condensation of these important subjects apparently to conform to a restricted size. It was a disappointment not to have found recorded some facts as to the nutritional and general disorders of infants incidental to four years of war diet and abnormal living conditions.

A. E. S.

A Dictionary of Treatment. By Sir William Whitla, M.A., M.D., LL.D., M.P. Late Professor of Materia Medica and Therapeutics in Queen's University, Belfast; Consulting Physician to Royal Victoria, Belfast Ophthalmic and the Ulster Hospitals for Women and Children. Sixth edition. Pp. 1083. Chicago Medical Book Co., 1920.

The appearance of the sixth edition of this book, and the fact that this present edition brings the total number of these books printed up to 32,000, shows that the presentation of therapeutics in this form is decidedly popular. The treatment of every conceivable condition is given some space in the book whether the condition is orthopedic or surgical, or whether it belongs to the realm of the dermatologist or to the internal medical man. As evidence of a large and diverse number of subjects treated we might mention the first three and the last three subjects that are indexed. They are respectively: Abdomen (gunshot wounds of); abortion; abscess; and writers' cramp; yaws; yellow fever.

The dictionary is carefully and conscientiously prepared and satisfactorily abbreviated. Necessarily in the short space that is at his command the author can devote only a relatively brief paragraph to any given subject; for example under fractures, only

the general principles of treatment are given, a procedure which is eminently wise. The one disadvantage of the book to the American physician is the frequent mention of drugs or other preparations which are not in the American *Pharmacopeia*. It must not be forgotten also that the strength of some of the preparations differ in the British and American *Pharmacopeias*. J. H. M., Jr.

The Oxford Medicine Advance Pages. Edited by Henry A. Christian and Sir James Mackenzie. Volume I, Part V. Pp. 635; 23 illustrations. New York: Oxford University Press, American Branch, 1920.

Part V, Volume I, of this *Oxford Medicine* series may be said to deal almost entirely with methods of diagnosis and their application to clinical medicine. The first 66 pages are prepared by Dr. Barker, who has written a delightful essay on a subject which is of interest to every clinician. He describes for us the ideal methods of arriving at a diagnosis in the presence of some hypothetical condition. Dr. Baker is extremely thorough in his study of the patient, and shows us that to appreciate completely the normal and the abnormal of an individual is beyond the scope of any one man, and therefore it is necessary to depend upon others for the more special examinations. This brings up the question of the so-called group medicine, which Dr. Barker, needless to say, advocates most heartily. He particularly stresses that opportunity should be given the great middle class to benefit by such an organization of medical men. At the present time the cost of these examinations is prohibitive to people in the average walk of life, therefore combination should be formed which, by proper business methods, could carry on this work for nominal charges.

Dr. Henry A. Christian has written the succeeding ten pages; a general summary of the functional tests, which have proved of some value in medicine. This chapter is a short one, and as Dr. Christian says, it is chiefly to indicate the underlying principles and the scope of these tests.

Respiration in disease, the next chapter, is presented by Dr. Francis Peabody. This article will probably repay the reader by careful study, as it is upon a subject which we are not accustomed to consider carefully in disease, and yet withal it is a subject which is not only intensely interesting but also of great value in considering not only diseases of the lungs and disturbances of pulmonary function, but also in many other conditions.

The last chapter is by Dr. Du Bois. It is upon the subject of the study of diseases with calorimetric methods. As with the other authors in this present portion of Volume I, Dr. Du Bois

is a recognized authority in his subject. In fact, it is doubtful if there is anyone who could have prepared a more authoritative article than Dr. Du Bois, who has done a tremendous amount of research and investigative work in this interesting study of the heat production and loss by the body. The article describes the methods of calorimetry and their application to the study of disease in such a clear and lucid style that there can be no doubt but that all who read will understand this rather complex subject.

J. H. M., Jr.

A Text-book of Dermatology. By J. Darier. Physician to the Hôpital Saint-Louis; Member of the Academy of Medicine, Paris, France; Honorary Member of the American Dermatological Association, etc. Translated from the second French edition. Edited with notes by S. Pollitzer. Pp. 769; 204 engravings and 4 colored plates. Philadelphia and New York: Lea & Febiger, 1920.

The author has made the present volume as concise and practical as possible, while including the entire domain of cutaneous pathology In order to make it short, he has sacrificed the entire bibliography, historical references, quotations, learned discussions, etc., limiting himself to the essential data from the standpoint of diagnosis and treatment.

The work is divided into two portions: Morphology of the Dermatoses and Nosology of the Dermatoses. The first twenty-two chapters are dedicated to the principal elementary dermatologic forms and to the syndromes derived from them. The author believes that the study of skin diseases should afford the first place to morphology—namely, to what can be seen. Eruptive dermatoses are first discussed from four angles: relating to efflorescence, to the eruption, to the disease and to the patient.

Under the name of elementary dermatologic forms, diseases of the skin of a variable morphology having various types of eruptive lesions on the one hand and of pathologic conditions of the skin on the other are discussed. Certain diseases having the same anatomic lesion, such as papules, vesicles, keratoses, etc., have been grouped together to show their resemblances and dissimilarities. Repetition would be a marked feature if the author had attempted to combine in contrast all the diseases of the skin having lesions of the same type as many conditions have a multiform eruption. In order to avoid this difficulty only the common and most characteristic syndromes are described in the first part of the volume, the others are mentioned briefly and their description follows in the second portion of the book.

Diseases such as eczema, lichen and psoriasis, the causes of which are multiple, complex or unknown, have been described in the first part of the work.

In the second part (Chapters XX to XXI) of the volume the pathologic entities, with a definite etiology, are classified according to the nature of their cause. The writer has placed the tumors of the skin under this heading, admitting that he conforms more to custom than following a personal conviction on the subject.

The arrangement of the volume, as is shown by the preceding description, is unique. The author states that, unfortunately, in the present stage of investigation the logical and scientific classification—namely based on etiology—cannot be followed.

The editor and translator, Dr. Pollitzer, of this work has added greatly to the elucidation by his expositions and additions.

Therapeutic notes are added as a separate chapter, giving the essential data required for dermatological treatment. A perusal of this section is interesting as showing the differences as to drugs and combinations as employed by the French and ourselves.

The text is good, the photographs excellent and the author is to be congratulated upon his work. F. C. K.

RAMBLING RECOLLECTIONS. By A. D. ROCKWELL, M.D. Pp. 332; 4 illustrations. New York: Paul B. Hoeber, 1920.

IT is refreshing at times to browse in the fields of endeavor of a brother in the profession, especially one who is honest enough to tell of failures as well as of successes, of disappointments as well as of hopes fulfilled.

Dr. Rockwell's childhood and early youth are entertaining. One can then follow him through his student days. In the section of the book called "A Ride with Sheridan," is a rather vivid description of a young army surgeon in the Civil War. These chapters offer an opportunity for comparison and contrast with the experiences of those who served in the recent war. One chapter in the book deserves special mention, because it gives the history of electro-execution in which subject Dr. Rockwell was deeply interested and with which he had official connection, due to his reputation as a physician versed in the medical use of electricity. In the last section of the book one finds sketches about many well-known men with whom Dr. Rockwell came in contact. A. G. M.

PROGRESS
OF
MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL AND NORTHEASTERN HOSPITALS AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

Pathology and Treatment of Grip Empyemata.—Beust (*Mitt. a. d. Grenzegeb. d. Med. u. Chir.*, 1920, xxxii, 94) says that grip empyema differs from the ordinary empyema in the greater virulence which is shown by the disease. This is seen in the rapid development of threatening symptoms and the high mortality. There is also a special inclination to fibrin formation, irregular temperature and recurrence of the primary lung affection. The abundance of fibrin formation hinders considerably the after-treatment of the empyema. The Bülau (suction) drainage is not sufficient alone to cause secure healing even if it is employed early, *i. e.*, as soon as possible after the appearance of the suppurative pleurisy. However, the Bülau drainage is especially valuable in relieving patients who are in very bad condition because of the grip pneumonia and empyema. Cases in which there is an extensive discharge on account of the development of a pneumothorax may be prevented by a two-stage operation. After the employment of the Bülau drainage in the first stage the patients so far recover that after several days, usually four to eight days, they tolerate a thoracotomy with rib resection. Primary rib resection should be employed in all cases that are in a fit general condition. The pus contains much fibrinous masses and can be drained thoroughly only by such a thoracotomy with rib resection. The surgeon should be in charge of the case whether the Bülau or rib resection drainage is employed. In the most severe cases in which the grip empyema becomes suddenly threatening, the Bülau drainage may be employed by the medical man as an emergency measure to good advantage, provided the proper technic is employed.

Observations on Empyema.—Ashhurst (*Annals of Surgery*, 1920, lxxii, 12) reports an excellent study of 43 cases of empyema and pays particular attention to the finding of concealed collections of pus and to dependent drainage. In his exploratory thoracotomy he places the patient in the fully prone position, under local anesthesia makes the

incision over the eighth or ninth rib and resects subperiosteally the desired length of the rib. As a rule 8 to 10 cm. is sufficient. The pleura is opened between forceps, like the peritoneum. The lung is usually adherent and does not collapse. Even if not adherent it seldom collapses to less than half its bulk, when the patient is lying prone, and there is comparatively little respiratory disturbance. Next inspect the structures closely. The lung may be so closely adherent to the diaphragm that it will be very difficult to recognize the line of junction. Wall off the rest of the pleural cavity with moist gauze. Then with fingers, dissecting forceps, or even knife and scissors (according to the density of the adhesions) the lung should be gently released. Usually it is well to clear the diaphragm first. If no pus is found here, the packs are rearranged so as to protect the lower part of the pleural cavity, and a search is begun in the fissures of the lung. The lung is absolutely insensitive to these manipulations. When pus is finally located and has been evacuated, a rubber tube (with a lumen of at least 1 cm.) surrounded with loose iodoform gauze is placed in the abscess cavity, the isolating packs are removed, and the wound is closed in layers, but not too tightly, around the drainage tract—the pleura and intercostal structures in one layer, and then the skin. He concludes that cases of pleural effusion suspected of being purulent should be punctured (with a hollow needle attached to a tight syringe) and if the effusion is massive most of it should be removed by aspiration one or two days before thoracotomy is undertaken. If the fluid found on puncture is serous or seropurulent, thoracotomy may usually be postponed, until frank pus has formed, as this delay will permit the formation of firmer adhesions and thus prevent complete collapse of the lung when the empyema is opened. Cures of such seropurulent effusions have so rarely occurred without final resort to thoracotomy that attempts to cure them by injection of antiseptic fluids into the unopened pleura are usually detrimental to the patient. If in a case of a suspected empyema the symptoms are urgent, but pus cannot be found by puncture, exploratory thoracotomy should be undertaken in an effort to locate and drain the pus. The operation of thoracotomy for empyema should provide free and dependent drainage, secured by the resection of a rib, usually the ninth, tenth or eleventh, in front of its angle. This operation may be done with perfect satisfaction to both patient and surgeon under local anesthesia, and in most cases this is preferable to a general anesthetic. Postoperative irrigations are unnecessary, unless after several months the lung shows no tendency to expand, when the use of Dakin's fluid may prove beneficial. In selected cases (those with small cavity) injections of bismuth paste may procure closure of the sinus. If the cavity cannot be made to heal by these means, the surgeon should do a major thoracotomy, combined with decortication of the lung and discission of the pleura, and in some cases resection of a number of ribs to permit the chest wall to collapse in part and meet the expanding lung.

Some Principles Involved in the Treatment of Empyema.—GRAHAM (*Surg., Gynec. and Obst.*, 1920, xxxi, 60) says that his appointment as a member of the Empyema Commission enabled him to observe an unusually large number of cases, and this opportunity was supplemented

by being placed in charge of 138 cases of chronic empyema at Fort Sheridan, Illinois, upon his return from France, in May, 1919. He has tested out by experiment the soundness of the principles advocated by this Commission and challenged by some as unsound. He summarizes his work as follows: The extensive recent literature on empyema reveals both a striking tendency toward more or less standardized treatment and a radical departure from methods in use prior to the war. He discusses the cardinal principles of (1) the avoidance of an open pneumothorax during the acute pneumonic stage of the disease; (2) early sterilization and obliteration of the cavity, and (3) the maintenance of the nutrition of the patient. In the normal thorax the mediastinal structures are so mobile that their resistance is negligible from the standpoint of pressure relationships so that the thorax can be considered as one cavity instead of two. Any change of pressure in one pleural cavity will manifest itself to practically the same degree in the other pleural cavity with the result that both lungs will be about equally compressed. The situation in this respect is the same in the dog as in the human, and, therefore, experimental results obtained on the dog can be directly applied to the human. The likelihood of a fatal asphyxia as a result of an open pneumothorax depends upon a number of factors, important ones of which are the size of the opening and the vital capacity of the individual. A mathematical expression has been devised by which it is possible in a given case to approximate the nonfatal opening in the chest wall if the vital capacity is known. One who has an average vital capacity (3700 cubic centimeters) and a normal thorax can withstand an opening in the chest wall of 51 square centimeters (8 square inches), but the individual of exceptional vital capacity (as, for example, 7100 cubic centimeters), can live with an opening of 101 square centimeters (15.6 square inches). A bilateral open pneumothorax is practically no more dangerous to life than a unilateral opening provided that in each case the areas of the openings are the same. These observations have a very important bearing on the question of open drainage of cases of empyema, particularly during the acute pneumonic stage when the vital capacity is low. After adhesions have formed and the mediastinum has become somewhat stabilized, both by adhesions and inflammatory induration, then the pressure relationships may be materially different on the two sides. Collapsing thoracoplastic operations have the disadvantage, even when successful, of apparently permanently reducing the vital capacity.

Chronic Paroxysmal Trigeminal Neuralgia and Its Treatment.—Harris (*British Med. Jour.*, May 22, 1920, 693) says that in the last twelve years he has had 312 cases. Only a comparatively small number get relief from drugs. Practically the only two methods of relief are gasserectomy and alcohol injections. The former operation should never be undertaken until alcohol injection has been thoroughly tried. During the last ten years Harris has injected the Gasserian ganglion 63 times. In 31 the anesthesia has remained total and no recurrence of pain has taken place. In many of the remainder partial ganglion anesthesia has persisted though pressure could be felt, yet the relief from pain appears to be equally good. In many cases, though total ganglion anesthesia is produced at the time of injection, yet the anes-

thesia of the first and second divisions wears off, perhaps completely, in from ten minutes to an hour, though the third division remains totally anesthetic. In such a case pain is liable to recur after two months or two years, as in a case of ordinary injection of a nerve. With total destruction of the ganglion there is the same liability to keratitis as with the operation of gasserectomy, but if the lids are kept carefully closed by strapping for the first week and the conjunctival sac washed out with boracic lotion twice a day, there will be little or no trouble. Hutchinson's partial gasserectomy avoids the danger of keratitis but is not a certain permanent cure, as Harris has seen three such cases relapse with neuralgia. In almost every case, as soon as anesthesia develops from the injection, the neuralgic pains cease, and they can no longer be started by any chewing movements or rubbing the face. The duration of the cure rarely lasts less than twelve months, if good anesthesia has been obtained, and in the majority the relief of pain lasts from two to three years. Very many of Harris' cases have been free for four or five years, one six and a half years, another seven years, another nine years after nerve injection only. No trophic effects on the skin are ever seen. Keratitis is a risk if the cornea is anesthetic after injection of the ganglion, but this may always be avoided by proper precautions.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

NEW YORK,

AND

CHARLES C. LIEB, M.D.,

ASSISTANT PROFESSOR OF PHARMACOLOGY, COLUMBIA UNIVERSITY, NEW YORK.

A Collective Investigation of 10,000 Recruits with Doubtful Heart Conditions.—Report IV. Compiled by S. R. WELLS (*British Med. Jour.*, May 29, 1920, p. 730). The following is the author's summary: Taking aortic regurgitation and mitral stenosis as the two typical valvular lesions which can be diagnosed with comparative certainty during life, the results of the present statistical inquiry lead us to the following conclusions: (1) The most important etiological factor in the production of organic lesions of the heart valves in men between the ages of eighteen and forty-one is rheumatic fever. (2) Strain can independently produce aortic regurgitation. (3) While strain may be a cause of mitral stenosis, it is a much less important factor than in the production of aortic regurgitation. (4) There is a third agent giving rise to symptoms simulating influenza, which is an efficient cause of mitral stenosis, and can possibly affect the aortic valves as well, but is not nearly so likely to do so. We have been unable to find any statistical evidence that syphilis, scarlet fever, diphtheria, pneumonia, or gonorrhea, are causes of valvular lesions, nor can we find statistical evidence that a history of

growing pains points to affections productive of valvular lesions. The same may be said, with slight reservations, of a history of rheumatism where there is no clear account of pain, swelling of the joints, fever, or confinement to bed. The evidence in favor of chorea as an efficient cause of mitral stenosis is strong, and we have found some, though not very striking, evidence in confirmation of the view that chorea and rheumatic fever are both manifestations of the activity of a common cause.

Experiences with Luminal in Epilepsy.—GRINKER (*Jour. Am. Med. Assn.*, 1920, lxxv, 588) found luminal in small doses (1.5 to 2 grains), once or twice daily, capable of arresting the convulsions of epilepsy. Larger doses are seldom required but may be given with safety. Large doses may be administered when beginning treatment, especially after sudden withdrawal of bromide treatment; even in such cases the dose may be gradually reduced to 1.5 to 2 grains. Luminal does not appear to be habit-forming and no harmful effects have been observed from its long-continued administration. Patients receiving average doses of luminal do not show the peculiar mental torpor of those taking bromides.

The Physiological Action of Fumes of Iodin.—LUCKHARDT, KOCH, SCHROEDER and WEILAND (*Jour. Pharm. Exp. Therap.*, 1920, xv, 1). Iodin deposted on the skin in the form of fumes is absorbed and appears in the urine of both man and dogs. In dogs the iodin content of the thyroid was found to be greatly increased, the increase being accompanied by a corresponding change in the histological features of the gland. The same was true when the iodin was inhaled. The inhalation of iodin fumes causes respiratory disturbances consequent on the irritant action of the fumes; large amounts lead to the death of the animal within twenty-four hours from acute and rapidly developing pulmonary edema. The edema supervenes more rapidly in animals having respiratory disease than in normal dogs. The authors believe that the fumes of iodin should never be inhaled for therapeutic purposes and in persons with pulmonary disease such administration is absolutely contra-indicated.

The Stability of Digitalis-leaf Extracts. The Infusion (Second Paper).—POMEROY and WEYL (*Am. Jour. Pharm.*, 1920, xcii, 394). A comparison of the relative activity of digitalis infusions and tinctures of equal concentration shows the infusion to be slightly less active. Placing a 20 per cent. limit on deterioration, the authors conclude that the infusions should be discarded in from three to five days' time; at lower temperatures the time limit may be extended to from six to seven days. In addition to the instability of the infusion itself, a wide variation in the strength of various samples of leaves was found. The addition of alcohol did not add to the stability of the infusion.

Botulism from Canned Ripe Olives.—EMERSON and COLLINS (*Jour. Clin. and Lab. Med.*, 1920, v, 559). Within the last six months there have been at least five small outbreaks of botulism in this country, due to the eating of canned ripe olives. Four of the five outbreaks were due to B. botulinus of the Boise Type (Type A). While Dickson's

recent work has definitely demonstrated the protective value of antitoxin when administered soon after the toxin, it must be remembered that antitoxin for one type is specific for that type alone. The authors recommend adequate government supervision of the plants (including fish packing and canning plants) for protection against B. botulinus contamination.

Gastric Response to Foods. X. The Psychic Secretion of Gastric Juice in Normal Men.—MILLER, BERGEIM, REHFUSS and HAWK (*Am. Jour. Physiol.*, May, 1920). The sight, taste and smell of appetizing food was found to give rise to a distinct secretion of gastric juice in normal men. Evil odors depressed secretion. Nourishing foods unpleasantly prepared and served sometimes caused a slight delay in evacuation time but none in acid response. The ultimate utilization of the protein of a diet prepared in a most unpalatable manner was not found to be appreciably less than that of the same diet served under the best conditions. Anxiety and mental strain markedly delayed gastric digestion.

Gastric Response to Foods. XI. The Influence of Tea, Coffee and Cocoa upon Digestion.—Water, tea and coffee, in 1 liter amounts, were practically without effect on the evacuation time of a uniform mixed meal; the rise of the level of intragastric acidity was somewhat delayed, as compared with the basal meal alone. Cocoa, in 1 liter amounts, distinctly delayed the evacuation time and the development of intragastric acidity. Tea and coffee in these amounts caused acceleration of the heart-rate, vasomotor relaxation, tremors, etc. Urine secretion after tea or coffee ingestion varied from 550 to 860 c.c.; after cocoa, from 125 to 370 c.c.

Vitamine Studies. V. The Antiscorbutic Propertics of Raw Beef.—DUTCHER, PEARSON and BIEST (*Jour. Biol. Chem.*, 1920, xlii, 301). Water extracts of raw, lean beef did not delay the onset of scurvy or increase the length of life of guinea-pigs fed on a "scorbutic" diet. Orange juice prevented scurvy, whether meat extract was fed or not. From the excellent condition of the animals on the orange-juice beef extract diet, the authors conclude that the scurvy was due rather to the absence of the antiscorbutic vitamine than to any deleterious property of the beef extract.

PEDIATRICS

UNDER THE CHARGE OF

THOMPSON S. WESTCOTT, M.D., AND ALVIN E. SIEGEL, M.D.,
OF PHILADELPHIA.

Sino-Atrial Heart Block in a Child.—BROWN (*Arch. Int. Med.*, September, 1919) discusses the case of a boy aged eleven years, in whom there was found the arrhythmia, which is usually called sino-auricular

block. There was a complete standstill of the entire heart for one or more beats, the intermissions being separated by from one to six normal cardiac cycles. The blocks which characterize the records from this patient may have hypothetically resulted from a failure of the sino-atrial node to generate an excitation wave, from a failure of the atrial musculature to respond to the excitation, or from interference with the impulse in its passage to the atrium. The persistence of a fundamental rhythm underlying this arrhythmia was the evidence of the maintenance of rhythmic impulse production. There was no evidence of diminished atrial excitability, and the atrium responded to every excitation wave when the rate was much augmented. The arrhythmia was best explained by the existence of some factor which interfered with the transmission of correctly timed excitation waves. Such a functional defect may be dependent either on structural changes or the influence of the depressor nerve. The records from this case presented some of the characteristics of functional block due to structural changes. After several contractions an impulse failed to pass. In the series of normal beats the atrial cycles preceding an intermission were slightly longer than those which followed it. This suggested an increasing delay in impulse transmission prior to the appearance of the block. Sinus-arrythmia associated with sino-atrial block is due to a progressive delay in impulse transmission according to Levine. Were this hypothesis applicable in this case a retardation in the rate of impulse production would eliminate and an acceleration would increase, the block. The rate was reduced and the block was eliminated by holding the breath after deep inspiration, but when stronger vagus stimulation was employed directly by pressure on the right vagus, or indirectly by ocular pressure, the intermissions increased in frequency. The administration of $\frac{1}{75}$ grain of atropin increased the rate to 120 per minute, but with acceleration the blocks disappeared. It was evident that if there was any structural defect in this case, it was a minor factor, and that the abnormal rhythm was due chiefly to vagus influence. The action of small doses of atropin in eliminating the arrhythmia without producing sufficient vagal inhibition to permit the acceleration of the impulse production, and the persistence of this slow, regular rhythm were of clinical interest. They indicate a prolonged primary atropin effect, which moderately stimulates the vagus center and retards impulse production, while coincident with this is a selective peripheral action of atropin on the vagus endings, which control impulse transmission, thus facilitating the passage of excitation waves to the atrium.

Mental Changes in Children of Germany.—BLANTON (*Mental Hygiene*, July, 1919) reports that at least 40 per cent. of the children in the Volksschulen of Trier, Germany, are suffering from malnutrition of such a degree as to cause a loss of nervous energy. There was no increase in the percentage of cases normally found of neuroses, psychoses, abnormal nervousness, organic nervous disease, tics, or conduct disorders. There was an increase of the number of borderline defectives totaling not more than 1 per cent. of the total school population. There was no increase in the percentage of the speech defects, especially stuttering, normally found, but there was a marked increase in poor lisping slurring speech due to the retardation or interference with the

fine coördination necessary for good speech, caused chiefly by malnutrition. The percentage of children failing to pass their grades was increased from an average of 8 per cent. in pre-war times to 15 per cent. in 1917 and 1918. About half of this 1 per cent. increase in retardation was due to malnutrition and the other half was due to war conditions. There was a lowering of the whole standard of school work caused chiefly by malnutrition, but partly by war conditions in general. Half of the children who in pre-war years did superior work, now do average work and the percentage of children who do inferior work was increased from 20 per cent. to more than 30 per cent. The specific changes noted in the children caused by malnutrition were: inattention during school hours; a lack of nervous and physical energy; poor and slow comprehension for school tasks; poor memory for school work; general nervous restlessness while in school. Children of good nervous stock and of superior or good average intelligence can withstand malnutrition of even a serious degree extending over more than two years without any impairment of the intelligence or any definite emotional change; a lack of nervous energy was about all the change that occurred. Those of poor nervous stock with poor or inferior intelligence suffer a general and sometimes a permanent lowering of the whole intelligence from even a moderate degree of malnutrition. Not more than 5 per cent. of the total school population suffered injury to the nervous system such as to affect the intelligence permanently. Conditions in Trier were not typical, having been worse than those in general throughout the Rhenish province as judged from the condition found in the cities of Cologne, Coblenz and Bonn.

Calcium Metabolism of Infants and Young Children and the Relation of Calcium to Fat Excretion in the Stools.—Holt, Courtney and Fales (*Am. Jour. Dis. Children*, February, 1920) estimate that the average of calcium oxid by healthy infants taking modifications of cow's milk is 0.09 gm. per kilogram of body weight. Since the average absorption of calcium oxid by breast-fed infants is about 0.6 gm. per kilogram of body weight, it may be assumed that 0.06 gm. per kilogram of body weight is the minimum normal absorption by infants taking modifications of cow's milk The daily average total excretion of calcium oxid in the stools range from 0.34 to 1.06 gm., with a mean of 0.70 gm. The excretion and the absorption of calcium were in general dependent on the amount of calcium intake, from 35 to 55 per cent. of the intake being absorbed. To insure the average absorption of 0.09 gm. of calcium oxid per kilogram, the intake of calcium oxid should be at least 0.19 gm. per kilogram and to insure absorption equal to the average found for breast-fed infants the intake should be at least 0.13 gm. per kilogram. The best absorption of calcium was obtained when the calcium intake bore a definite relation to the fat intake, or when the food contained from 0.045 to 0.060 gm. of calcium oxid for every gram of fat, and when at the same time the fat intake was ample, not less than 4.0 gm. per kilogram. An excessive calcium intake apparently did not increase the calcium absorption, the excess being excreted. When the intake of calcium oxid was very low, less than 0.10 gm. per kilogram the absorption of calcium oxid was less than the normal calcium requirement of the body. The total absorption of calcium oxid

varied in general with the weight of the child; the per kilogram absorption did not vary regularly with either the age or the weight. The relation of calcium excretion to soap excretion was not constant. The excretion of soap was directly related to the type stool, that is, to the water content and to the reaction of the stool. The excretion of calcium was closely related to the calcium intake. On the average, the normal and the constipated stools, with high soap content, were found when the intake of calcium was high, and they showed the higher excretion of calcium. Constipated stools, which contained more soap than normal stools, had lower calcium content. Non-homogeneous stools, with the lowest average soap content, showed the same amount of calcium not held as soap as did the constipated stools, with the highest soap content. The calcium that could be lost as soap was never a large proportion of the calcium intake. Even in the stool containing the most soap it was found to be less than three-tenths the calcium intake. The calcium lost as phosphate was shown not to be increased in soapy stools. The calcium percentage of the total solids varied with the water content of the stools, diminishing as the water increased. The calcium absorption was much lower when diarrhea was present. With an increased excretion of calcium in diarrheal stools, there was a marked decrease of soap excretion. The calcium of absorption by rachitic infants was much lower than in healthy infants. In the few cases in which the authors made observation on infants recovering from rickets, the calcium absorption was higher than the average. The infants had received cod-liver oil for a considerable time. The administration of cod liver oil regularly increased the absorption of calcium, unless diarrhea was present.

Atropin Treatment of Pylorospasm and Pyloric Stenosis.—Haas (*Arch. Ped.*, October, 1919) says that hypertrophic pyloric stenosis is probably only an advanced degree of pylorospasm. Both of these conditions are seen in the syndrome of hypertonia or in the hypertonic infant. The cause is probably in a disturbance of the physiologic action of the vegetative nervous system. This is made up of two parts, the autonomic and the sympathetic. These are normally in balance, but in this condition there is an overaction of the autonomic and there arises a condition of vagotonia. Although this is usually the case, there also occasionally exists a true organic stenosis of the pylorus. Many brilliant results have been obtained by the Rammstedt operation, but in this condition an operation should be rarely required and should only be done after atropin has been given a trial. When properly used this has been regularly effective in producing a cure. At present most authorities agree that hypertrophic pyloric stenosis and pylorospasm are two different clinical entities. In favor of this view is the existence of a cartilaginous hard mass of the pylorus in cases of stenosis, and the persistence of this mass long after a cure has been obtained by operation or otherwise. Among the arguments for non-medical treatment is the sudden death which not infrequently occurs. These are usually thymus deaths, and occur in cases operated as well as in those treated medically. Atropin is the logical treatment in these cases owing to its paralyzing effects upon the vagus nerve endings. There must be borne in mind that atropin is inconstant in value, resembling digitalis

in this respect. It deteriorates rapidly, and it must be used in doses sufficiently large to be effective. A common dose for an infant of this type from a few weeks to a few months of age is $\frac{1}{50}$ to $\frac{1}{25}$ grain in twenty-four hours, with an extreme of $\frac{1}{16}$ grain divided among the days' feeding. A solution $\frac{1}{1000}$ is used beginning with one drop and increasing rapidly until effective. The most frequent toxic symptoms are flushing midriasis, dryness, which disappears promptly when the drug is withdrawn. No danger exists even when these symptoms are present.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Pregnancy and Labor following Amputation of the Cervix Uteri.—PAVLIK (*Surg., Gynec. and Obst.*, August, 1919) writes a paper upon this subject in which he quotes the experience and opinions of various obstetricians, all tending to show that amputation of the cervix is followed during pregnancy and labor by complications of varying severity, which may even require the performance of Cesarean section and labor for the safe delivery of the patient. He describes the case of a woman, who had a very difficult confinement, in which pubiotomy was done and a twelve-pound child extracted that lived twenty-four hours. The patient was badly torn and six months later the cervix was amputated. This patient came under observation in the fourth month of her third pregnancy. The cervical scar was a hard, inelastic ring which did not soften. Fearing that the patient would go into labor with a disastrous result, Cesarean section was performed about two weeks before full term. The patient was sterilized by resection of the Fallopian tube before the abdomen was closed. Mother and child made a good recovery. He also describes the case of a woman who had a very difficult forceps delivery, followed by abortion and afterward by the amputation of a badly lacerated cervix. Since this operation she had three abortions at six and a half, four and three months. When seen she was in the third month of her sixth pregnancy and shortly afterward aborted. At the time of writing the patient was again about two months pregnant and refused operation and sterilization. The study of statistics shows that sterility is not uncommon after amputation of the cervix; further, less than 20 per cent. of these patients conceived after the operation. These results are cicatricial contraction, stenosis at the internal os and perhaps other changes. It is estimated that 5 per cent. of these patients abort when pregnancy follows the operation. Sixty-four per cent. had serious dystocia while in 128 cases but four had easy labors after the operation. Unquestionably the cervix has a function in closing the uterus at its lower extremity and thus preventing premature evacuation. The absence of this safeguard may

well explain the frequency of abortion after the cervix has been removed. Studiford recommends that if amputation be done during the child-bearing period the operation should not extend higher than half an inch below the internal os. This would exclude the original technic of Schroeder. In discussion, Paddock stated that in his experience abortion had occurred most frequently from the diseased condition of the endometrium rather than the anatomical change produced by the operation. He could not believe that abortions which occurred early are due to amputation of the cervix. He could well see how amputation could produce premature labor. In his experience labor at term without serious complications have followed the operation. Heany called attention to Martin's operation, which is a low amputation, with just a portion of the cervix removed. He has seen successful labor follow this operation twice in the same patient. In the experience of the reviewer premature labor developed in a case in which amputation of the cervix had been done. Spontaneous dilatation failed and it was necessary to complete dilatation by artificial methods. In the second case there was long delay in the first stage; labor was finally terminated by manual dilatation and extraction by forceps. In two other cases Cesarean section was the only means of successful delivery, because the mass of cicatricial tissue of the cervix made delivery through the cervix impossible.

Influenza Complicating Pregnancy.—HARRIS (*Jour. Am. Med. Assn.*, 1919, No. 72, p. 978) has studied 1350 cases. This number did not include the very mild cases or many which occurred during the first months of pregnancy when the pregnant condition might readily escape detection. It was found that pneumonia complicated the influenza in about half of the pregnant patients. In these cases complicated by pneumonia the mortality was about 50 per cent. and this was seen especially during the last three months of pregnancy. The average mortality of all cases was 27 per cent. Pregnancy was interrupted in 26 per cent., and of these 52 per cent. developed pneumonia, abortion or premature labor. Thus in 38 per cent. of the fatal cases the patient died without the interruption of pregnancy, while in 62 per cent. of the pregnant cases pregnancy was interrupted. When pregnancy was not interrupted the mortality-rate was 16 per cent. When interruption occurred it rose to 41 per cent.

The Development of the Mammary Glands.—MEYERS (*Am. Jour. Dis. of Children*, 1919, No. 18, p. 4) calls attention to the development of the mammary gland in the embryo. It is first represented by a single layer of elongated epithelial cells extending on each side from the anterior to the posterior limb bud. By the proliferation of these cells resulting in the formation of several layers the mammary line is formed, slightly elevated above the epidermis. The growth of the cells continues only at intervals along the line. The intervening portions of the line gradually disappearing, and as the hillocks grow they sink into the subjacent tissue and begin to bud from their deeper surfaces. The buds which develop progressively and sink into the mesenchyma represent the future milk ducts. In men there are 15 to 20 primary buds in

each hillock. The lumen of the milk duct in man develops about the sixth or seventh month, caused by a rearrangement of cells. The lumen of the milk duct in man begins to develop about the sixth or seventh month, and is formed there by a rearrangement or by degeneration of cells. At birth the ducts show congenital branching and soon after birth secretion of milk appears in the milk ducts of human infants. This secretion, which may cause marked engorgement, is usually carried away by leukocytes or direct absorption within the next twenty days. In children prematurely born fluid may be present at birth and may not appear for many days or not at all. This contains all the constituents of true milk, but it has not been determined whether the stimulus which induces activity in the mammary glands of the mother is the same as that which excites the glands of the newborn to secrete what is called "witches' milk." The stroma of the mammary gland develops from remnants of the mesenchyma about the mammary hillocks. As these sink into the surrounding tissue their superficial surface becomes depressed below the level of the surrounding epidermis by a process of degeneration and a desquamation by which is formed the mammary pit. Very soon a small papule forms at the base of the pit, which is the beginning of the nipple, and this grows until it fills the pit. In many cases the nipples of newborn infants have not reached the surface of the surrounding epidermis. In others they fill the pit completely while in the remainder they are slightly elevated. Usually the nipples become elevated shortly after birth and are of adult form and size at puberty. In man each of the fifteen to twenty milk ducts has a separate milk core in the surface of the nipple. In 7 per cent. of human embryos supernumerary mammary glands develop along the course of the original mammary stream. In the lower animals the period of anemia and depression at an early age stops for a time the development of the mammary glands. When the animal is fed well the glands respond slowly. If the sexes be compared it is shown that "witches' milk" is secreted by both; up to puberty the milk ducts branch somewhat more in the female than in the male, and that in the male the mammary gland may show some growth after puberty while retrogressive changes are more apparent in the male gland after the thirtieth year.

Fats, Cholesterol and Sugar in the Blood During Pregnancy.—SCHILLER (*Surg., Gynec. and Obst.*, November, 1919) has studied thirty pregnant patients, examining their blood to determine the presence of fat, cholesterol and sugar. He finds that in the later months of pregnancy, or in the first two weeks of the puerperal period, there is no hyperglycemia. The glands of internal secretion and the kidneys offer an explanation for glycosuria and alimentary glycosuria. Where in pregnancy a patient grows excessively fat this is for the most part a condition of hyperlipoidemia. There is no direct parallelism between cholesteremia or the hyperglycemia of pregnancy. It is probable that the endocrine glands are to be considered an important factor in developing the action of the mammary glands. On one occasion, in the case of a patient nursing her infant, the breasts became unusually swollen and the mother succeeded in nursing her child. It was observed that nursing caused great irritation, and that gradually the mother was

becoming much excited and complaining constantly of the breasts. The secretion of milk was not very abundant. Finally fever developed, although the infant remained remarkably undisturbed. Thyroid extract was given the mother in full doses when her symptoms disappeared and mother and child did well. This is in keeping with the remark of the writer that the endocrine glands are responsible for many conditions pertaining to lactation.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA,

AND

FRANK B. BLOCK, M.D.,

INSTRUCTOR IN GYNECOLOGY, MEDICAL SCHOOL, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Disagreeable Sequelæ from Radium Treatment.—GRAVES (*New York Med. Jour.*, 1920, cxi, 969) recounts certain disagreeable sequelæ from intra-uterine radiation which, though mentioned by several writers, received minor attention or have been lost sight of in the reports of brilliant end-results. Some of these symptoms are significant chiefly from the psychological influence which they may exert on the patient, but even these may be of considerable import to the patient's general welfare. First among the specific symptoms from an intra-uterine application of radium must be mentioned nausea and Graves calls attention to our statement that "nausea and vomiting are the exception rather than the rule after radiation." His own experience has been rather the reverse for he finds that the majority of patients suffer more nausea than would be expected after a simple ether examination and curettage, in which the length of anesthesia would be approximately the same. That the nausea is due to something more than the simple effect of the anesthetic is often strikingly evident by the almost immediate relief that follows the removal of the radium in certain cases. In other cases the nausea has been persistent, with greater or less intensity, for a period much longer than is seen in even unfavorable cases after a short anesthesia, where radium has not been used. In some cases there is little or no nausea after radiation, but in his experience these cases are the exception, whereas after a simple curetting they are the rule. In one of his patients violent nausea and vomiting persisted for seven days after a mild dose. The patient, a strong young woman of twenty-seven, was neurotic and apprehensive, but the severity of the symptoms could not be explained wholly by her mental attitude, nor by the small amount of ether administered at the operation. A second important after-result of the radium treatment is a possible continuation or reappearance of the bleeding, for the cure of which the operation was

undertaken. Such bleeding may appear within a few hours after the removal of the radium, and may persist for days or sometimes weeks, with varying degrees of intensity and constancy, before permanent cessation takes place. The amount of blood lost varies from a steady profuse flow to an occasional scanty showing, and the time of its appearance may extend from two or three days to five or six weeks. To a nervous, apprehensive woman, not premonished of this possible event, and confidently expectant of an instantaneous cure, the continuation of symptoms comes as an alarming shock, and the attendant who has neglected to forewarn his patient finds it extremely difficult to explain conditions. In some cases, in patients treated for menorrhagia, the next one or two periods may show no diminution, and sometimes even an increase of the catamenial flow. Here again the attendant who has not cautioned his patient finds himself in a embarrassing predicament in his perfectly truthful assurance that the ultimate result will probably be entirely satisfactory. A third specific after-effect of intra-uterine radiation is leucorrhea. In cases of recurrent bleeding it seems to appear as the end-result of the flow in the form of a thin watery discharge of a pinkish hue which gradually fades to a pale brown or colorless character. In cases where the radium application has caused a complete cessation of bleeding the same watery discharge usually ensues for a varying length of time, lasting from a few days to several weeks or months. Some patients do not notice it at all but they are in the minority. It has been a matter of rather frequent personal observation that this characteristic radium leucorrhea appears periodically for several months at the usual menstrual time and seems to indicate an effort on the part of Nature to reëstablish the menstrual rhythm. The discharge is chemically irritating and if not properly treated by cleansing douches becomes foul and may set up an annoying vaginitis, as has occurred in more than one of his cases. Pelvic pain has been described by some as one of the typical symptoms following the radium treatment. There are occasional complaints on the part of patients of a slight nagging pain in the side, usually on the left, which has subsided in a few days and gives no further trouble. In a small number of cases patients suffer pain of a nature of a uterine colic during the time of the radium application, the result apparently of a reaction on the part of the uterus to a foreign body within its cavity. In a few other cases, however, the pain experienced during the immediate convalescence proved to be the forerunner of later very serious inflammatory consequences. In the light therefore of present experience, Graves is convinced that in the properly selected cases there should be no adnexal pain and that if it does occur, it must be regarded as a danger signal of grave import. Too great emphasis cannot be laid on the danger of making intra-uterine radium applications in the presence of pelvic inflammation. Even though the active inflammatory process existed years before and there remain only a few peritoneal adhesions radiation is attended with risk. Inasmuch as an old inflammatory process is sometimes missed both in the history and the most expert preliminary examination, it stands to reason that even with great care occasional results are sure to be encountered and anyone who says that the intra-uterine application of radium for bleeding is attended with no danger knows little whereof he speaks. The injurious influence of radium on chronic inflammatory

pelvic conditions, is perhaps the most important reason why in the extensive clinical use to which radium is destined very soon to be put, its employment, in gynecological practise at least should be limited to responsible and well trained operators. Some mention has been made in the literature of a reaction on the part of the kidneys to radiation. Graves has had an opportunity of observing in another clinic, the onset of an acute nephritis following an intrauterine treatment, in the case of an elderly woman who had a cardiorenal history. He has collected no specific data on this point in his series of cases, nor has he seen any systematic report throwing light on this subject. Nevertheless, there is sporadic evidence that caution should be exercised in treating cases with renal disease. Nervous symptoms following radiation are of peculiar interest. If the menses are inhibited, hot flushes are common but not constant. They occur in about the same proportion as after hysterectomy with or without the ablation of the ovaries. Some think they are less intense and annoying, others think they are more so. In his experience he cannot see that there is any marked difference one way or the other. They seem to follow the same law as after radical operations in that they are intensified by complicating discomforts and temporary disappointment over the result of the treatment. The influence of the ovarian secretion is strikingly illustrated in cases where, after a period of amenorrhea, the menses are reëstablished with a complete synchronous disappearance of hot flushes. As after hysterectomy, the hot flushes when present are usually amenable to ovarian therapy, preferably in the form of the residue or the whole extract. The various points brought out in this article are presented not for the purpose of depreciating the great value of radium in the treatment of non-malignant uterine hemorrhage, but rather to warn those who have not yet used it for this purpose that the immediate convalescence from a given treatment is by no means always a bed of roses.

OPHTHALMOLOGY

UNDER THE CHARGE OF
EDWARD JACKSON, A.M., M.D.,
DENVER, COLORADO,
AND
T. B. SCHNEIDEMAN, A.M., M.D.,
PHILADELPHIA.

Action of Hypophysin (Pituitrin) Upon the Pupil of the Rabbit.—Polleck (*British Jour. Ophthal.*, March, 1920, p. 106) finds that hypophysin (pituitrin), when instilled into the eye of the rabbit, produces a mydriasis in about 94 per cent. of the experiments, although it is necessary in some cases to repeat the instillations several times. The effect is increased by decentralization (*i. e.*, cutting the sympathetic in the neck below the superior cervical ganglion) and still more by

deganglionation (excision of the ciliary ganglion and accessory ganglia and the superior cervical sympathetic ganglion of the dilator pupillæ or of the sphincter pupillæ) and most markedly by deganglionation of both dilator and sphincter pupillæ. When hypophysin is administered by intravenous injection, the local mydriatic effect is lost if the blood-pressure is raised, when a miosis occurs, due to central stimulation of the third cranial nerve which relaxes with the return of the blood-pressure to normal, and is followed generally by slight dilatation. The constriction of the pupil may be preceded by a brief dilatation due to excitement at the moment of injection. When the third cranial nerve is interrupted by section above the ciliary ganglion and accessory ganglia, the pupil dilates within a few minutes of the injection and generally returns to its normal size within an hour. Hypophysin acts on the same structure as adrenalin, and since adrenalin acts on the neuromyal junctions, hypophysin must also act there. Since deganglionation does not cause degeneration of the terminal plexus, the presumption is that both drugs act upon this.

Experimental Study of Antigonococcic Serotherapy. — TERRIEN, DEBRE and PARAF (*Arch. d'Ophtalmol.*, June, 1920, p. 326) finds that injection into the anterior chamber of rabbits of an emulsion of gonococci causes an inflammation characterized by an iridocyclitis, torpid in evolution, with moderate pericorneal injection, but with great tendency to exudation, synechia and large hypopyon. The process continues from ten to fifteen days, terminates in total occlusion of the pupil with exudation into the pupillary field and partial cloudiness of the cornea. In a very small number of instances, the affection is milder as shown simply by a few synechia of the pupillary margin and slight discoloration of the iris with slight pericorneal reaction and little or no hypopyon. In rarer instances still, the disease is much more severe, manifesting itself by extreme reaction with considerable hypopyon, sometimes even perforation of the cornea and phthisis bulbi. The gonococci do not proliferate in the lesions noted, as, in fact, has also been remarked by various authors. Injection of 0.3 c.c. specific serum into the anterior chamber, twenty-four hours after preliminary inoculation, entirely modifies the evolution of the malady; the gravity of the lesions is much diminished, cure much more rapid (four to six days) and complete. Intramuscular, intravenous and subconjunctival injection of the serum is without influence upon the evolution of gonococcic ophthalmia; intra-ocular injection of antimeningococcic or antidiphtheritic serum is likewise inefficacious. The preventive power of the serum is doubtful; effects of intra-ocular injection twenty-four hours preceding injection of the microbes is uncertain. The favorable results of antigonococcic therapy confirm the observation previously made by these observers with the serum of immunized rabbits; but they do not justify any opinion upon the effects of serotherapy in man; in the case of the rabbit, the gonococci did not proliferate and the effect of the serum is reduced to an anti-endotoxic action.

Irregularity of the Pupil in Syphilis.—RASQUIN (*La Clin. Ophtalmol.*, June, 1920, p. 292) has studied the occurrence of irregularities of the pupil in syphilis. He attributes the greatest importance to the form

which the irregularities take—the form of widely extended angles, for the following reasons: this form represents a morbid entity which may be present in all stages of the disease. It is also the most frequent, constituting 79 per cent. of all syphilitic irregularities of the pupil. It also gives the minimum percentage of failures in determining the syphilitic origin of pupillary irregularities; of 100 patients affected with this form of irregularity, syphilis was certainly present in 74 and possibly in 89. He is of the opinion that this form of irregularity, particularly when bilateral, as an almost certain symptom of syphilis so that when present the serological reaction should always be sought.

Raising Ocular Tension.—LAGRANGE (*Annal. d'Oculist.*, July, 1920, p. 447) has attempted to raise the tension in eyes affected with high myopia and detachment of the retina. He has found in 17 of 52 myopes hypotension reaching 5 mm. Hg. After treatment normal tension supervened lasting several years in two-thirds of those operated upon. His procedure seeks to abolish the conjunctival meshes opposite the angle of filtration. This can be accomplished by repeated injection of cyanide or by a technic which he advocates and which consists in the destruction of the zone of conjunctiva surrounding the cornea adjacent to the anterior chamber, by cauterizing the tissues with the galvanocautery to bring about reaction and the production of a fibrous tissue. Hypertension usually supervenes the following day and lasts three or four days to give place to a renewed diminished tension, lasting a month, to be followed at the end of three or four months by increased pressure which finally becomes about normal. Fifteen cases of retinal detachments thus treated were cured.

Relation of Diseases of the Eye to Those of the Nose and Sinuses.—STEIGER (*Med. Klin.*, 1920, No. 9, p. 221) calls attention to the multiform and frequently intimate relations between diseases of the eye and those of the nose and accessory sinuses. Acute and chronic catarrhs of the conjunctiva often point to changes within the nose, which latter depend upon mechanical interference with normal nasal respiration, especially hypertrophy of the inferior turbinate. Scrofulous affections of the cornea and conjunctiva almost invariably indicate concomitant adenoid disease. The author believes that in such cases the symptoms are not simply concomitant, but that the nasal affection is to be regarded as the primary cause and as aggravating the ocular conditions; when the local symptoms of the nasal process are relieved, the ocular affection pursues a more favorable course. Acute inflammatory diseases of the orbit are due, in the majority of cases, to direct contact or conduction from an acute inflammatory process in the nasal fossæ. Frontal sinus, antrum, anterior and posterior ethmoidal cells and the mastoid may become involved whenever the narrow outlets of the nasal fossæ have been closed by disease, particularly acute swelling. Treatment consists accordingly in endo measures looking to prompt drainage of the diseased nasal fossæ. In chronic conditions, on the other hand, an independent focus of disease is frequently present in the sinuses, which is capable of further extension through erosion of the bones. Rational therapy demands removal of the primary focus of the affected sinus. Diseases of the lacrimal canal and sac may be excited by

swelling in the region of the inferior turbinate, whenever such swellings extend to and close the nasolacrimal outlet; dilatation of the latter also, as in ozena, may likewise cause disease of the lacrimal drainage apparatus through entrance of diseased products from the nose mechanically or by extension through continuity. The treatment in these cases is cure of the nasal affection. Dislocation of the globe by mucoceles and tumors are too well known to require special mention; the same is true of affections of the optic nerve. The possibility of reflex neuroses of the eye of nasal origin should also be borne in mind; proof of the rhinologic origin of cataract, glaucoma, etc., has not yet been furnished.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

OSKAR KLOTZ, M.D., C.M.,

PROFESSOR OF PATHOLOGY AND BACTERIOLOGY, UNIVERSITY OF PITTSBURGH, PITTSBURGH, PA.

Streptolysin.—Although the use of the blood-agar plate for the differentiation of alpha and beta hemolytic streptococci has become quite general, there has been a lack of uniformity of method and but little attempt at standardization. Impressed by the fact that the hemolytic zones surrounding colonies of the beta hemolytic streptococcus were wider and clearer on 10 per cent. sheep's blood-agar plates than on those prepared from similar concentrations of rabbit and human blood, DE KRUIF and IRELAND (*Jour. Infect. Dis.*, 1920, xxvi, 285) have studied hemolysin production by these organisms on blood accessible to general use, in order to ascertain whether variations in suitability exist among these bloods and to determine their optimum concentration for maximum production. Beef-infusion broth was employed in all cases, being adjusted to a hydrogen-ion concentration of pH 7.8. The investigations included studies on human, rabbit, sheep and horse blood. Instead of following the previously described methods of titration of filtrates or whole cultures the authors titrated the supernatants of early broth cultures seeded with from eight to twenty-four-hour cultures of hemolytic streptococci against constant quantities of the washed erythrocytes. Extensive experimentation was carried out, the results being recorded by tables and graphs. It was found that lysin production reached its maximum for the strains studied at a very early period in the life of the serum broth culture. When the serum broth was inoculated with young (eight to twelve hours) cultures this peak was reached in from seven to eight hours. In older cultures the crest may be deferred to twelve hours. Heated serums were usually superior to unheated ones. Sheep and horse serum were superior in all concentrations to human and far superior to rabbit serum broth. From the results of their experiments the authors devised a new blood-agar plate with the idea of using the optimum serum concentration for maximal lysin production of a blood both efficient and available. Sheeps' blood

was recommended, the serum-cell mixture being made by adding 1 part of cells to 4 parts of heated serum. This mixture was then combined with liquid agar in the proportion of 1 to 3, so that the final concentration was serum, 20 per cent.; cells, 5 per cent.; and agar, 75 per cent. This medium was found to be not only suitable for demonstrating the hemolytic zones of beta streptococcus but efficient in exhibiting the multiple concentric zones of green production and hemolysis for alpha streptococcus and pneumococcus.

Experimental Streptococcus Empyema; Attempts at Prevention and Therapy by Means of Vaccine and Serum.—The importance of streptococcus empyema has not only not decreased but has become intensified during the last year or so by its occurrence as a fatal sequel to influenza as well as in its previous relation to spontaneous bronchopneumonia and bronchopneumonia after measles. GAY and STONE (*Jour. Infect. Dis.*, 1920, xxvi, 265) undertook the present study not simply in an effort to proceed toward a possible practical method of treating streptococcic empyema, but in a desire to contribute some information to the larger question of streptococcic immunity as a whole. The experiments were conducted on rabbits by means of a single pure strain isolated from the lung of a fatal case of bronchopneumonia complicated by empyema and pericarditis, and though culturally of the S. pyogenes group, was immunologically unclassified. Beef infusion broth, pH 7.2 to 7.4, and containing either 1 per cent. glucose or 5 per cent. sterile fresh rabbit serum, was the medium employed. In counting the bacteria it was found that the Wright method, when checked by the gravimetric tests, gave accurate and consistent results. The particular strain was not markedly pathogenic for rabbits by intravenous inoculation. Attempts to increase the general invasive properties of the cultures for rabbits were unsuccessful, as were all attempts to produce bronchopneumonia by bronchial insufflation. Empyema could be procured, however, by injecting small quantities of broth cultures into the pleural cavity, particularly when subcultures from the pleural fluid of an animal with fatal empyema which had been passed through the pleuræ of several animals was employed. Death occurred in from one to seventeen days, the average being five days. Of 103 rabbits injected by a constant dose of a uniform passage culture, 102 showed involvement of one or both chests, with or without pericarditis. There was no evidence of an elective localizing affinity with the strain used. If sufficient amounts of killed and subsequently living cultures of streptococci were given over a considerable period of time, protection against empyema occurred. The total number of bacteria injected, rather than the number of injections, seemed to be the decisive factor. The immune serums produced gave positive agglutination reactions at 55° C. in dilutions of from 1 to 400 to 1 to 12,800. The technical difficulties were surmounted by using a constant homogeneous suspension, made by the addition of phenol in a final concentration of 0.2 to 0.5 per cent. to a twenty-four-hour serum broth culture. The serum of the animals in which active immunity had been proved by intrapleural inoculation was found to vary in tropin content from five to eighty times that of normal rabbit serum. Satisfactory precipitin reactions were obtained

by the immune serums used for therapeutic purposes, the antigens consisting of extracts of ground and dried streptococci. It was shown that the immune sera which contained strong antibodies may have a preventive and curative action when given before, with and after the infecting intrapleural dose of bacteria. Attempted vaccine therapy of the localized empyema gave consistently negative results. The authors conclude that although distinct results in the prevention of experimental empyema and, in rare instances, the cure of empyema may be produced by the use of immune serum from rabbits, they have as yet no evidence of an encouraging serum therapy to offer and that no optimistic conclusions can be drawn from their results as to the possibility of protecting human beings against localized streptococcus infections, or, specifically against empyema, owing to the large amount of vaccine and the prolonged nature of treatment required.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

MILTON J. ROSENAU, M.D.,

PROFESSOR OF PREVENTIVE MEDICINE AND HYGIENE, HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS,

AND

GEORGE W. McCOY, M.D.,

DIRECTOR OF HYGIENIC LABORATORY, UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.

Pellagra Incidence in Relation to Sex, Age, Season, Occupation and "Disabling Sickness" in Seven Cotton Mill Villages of South Carolina during 1916.—GOLDBERGER, WHEELER and SYDENSTRICKER (*Public Health Reports*, No. 28, XXXV, 1650) conclude their study by the following summary: "(1) During 1916 the incidence of pellagra among the members of the families of white mill operatives of seven representative cotton mill villages of South Carolina was included in our study. (2) In a population of 4399 a total of 115 definite cases, representing a rate of 26.1 per 1000, was recorded. If 73 cases with ill-defined eruption recorded as 'suspects' are included, there were in all 188 cases and an incidence rate of fully 42.7 per 1000 in this population. (3) The data appear to indicate that the disease is rare in children at the age of two and under; that among both males and females up to twenty years the incidence is similar, being higher among children between two and ten years than in persons of the ages of ten to nineteen inclusive; and that among adults twenty to fifty-four years old the incidence is many times higher in females than in males. (4) There was a sharp rise in incidence during April and May, reaching a well-defined peak in June. The season of onset appeared to be confined almost entirely to the six months April to September inclusive. (5) The pellagra rate among both males and females was considerably higher for the non-millworkers than for the millworkers. (6) While

the pellagra rate among non-millworking females was approximately four times as high as that among millworking females, the rate for disabling sickness appeared distinctly higher in millworking than in non-millworking females. The disability indicated by the higher sickness rate among millworking females appeared not to influence materially the pellagra rate in this group."

A Study of the Relation of Factors of a Sanitary Character to Pellagra Incidence in Seven Cotton Mill Villages of South Carolina in 1916.—GOLDBERGER, WHEELER and SYDENSTRICKER (*Public Health Reports*, 1920, No. 29, xxxv, 1701) conclude the study of their problem as follows: "This study of the relation of factors of sanitary importance to the incidence of pellagra in seven representative mill villages has failed to reveal any consistent correlation between them. Although based on a rather small mass of data and, in itself, not warranting any conclusions, it may, nevertheless, be noted as not without significance that this result, at any rate, affords no support for the view until recently, at least, quite widely entertained in this country, that pellagra is 'an intestinal infection transmitted in much the same way as typhoid fever;' nor does the evidence adduced in favor of this view by other workers, when rightly considered, afford it any real support. It may be of interest to add that the results of the very much more extensive study of this subject carried on by us during 1917 and 1918, to be presented in a later communication, are in harmony with and confirm those here recorded."

Absorption of Cyanide Gas by Foodstuffs.—The Public Health Service (*Public Health Reports*, No. 27, xxxv, 1597) has had a series of experiments made to determine whether there is any danger of poisoning from the use of foodstuffs that have been exposed to cyanide gas in the process of fumigation for the destruction of vermin. The experiments were conducted by exposing bread and milk to the gas and then feeding the exposed food to mice, and, as a result of the tests, it was considered that the danger was "exceedingly remote."

Can the Mosquito Convey Infection from a Malaria Patient Undergoing Treatment? Does Sporogony Affect Mosquito Life?—MAYNE (*Public Health Reports*, No. 28, xxxv, 1664) reviews the evidence on this subject, which indicates that the gametocytes taken with the blood of a patient undergoing quinin treatment develop in the usual manner and that transmission to a new human host may occur. The infestation of the mosquito host does not appear to be prejudicial to the life of the insect; this is in contrast with the high mortality of mosquitoes infested with microfilarial parasites.

Utility of Antiplague Vaccines and Serums.—MCCOY and CHAPIN (*Public Health Reports*, No. 28. xxxv, 1647) review the evidence of the value of biologic products in the prophylaxis and treatment of plague. The work of Haffkine and others is reviewed and the opinion is expressed that while vaccine is probably of some value it is not capable of controlling an outbreak of plague. The evidence on the prophylactic value of serum is not conclusive and the agent need not be seriously con-

sidered in this connection. The therapeutic use of serum is usually advantageous but brilliant results are seldom seen. The concluding paragraph of the paper is as follows: "It seems rather unfortunate to those who are called on for advice in connection with a plague outbreak to find that popular and professional interest is so frequently centered on the subject of prophylaxis by vaccines or serums and on treatment by serum when, in fact, the situation demands active measures against rodents. Under American conditions at least it is not a matter of much importance whether biological products are used in a prophylactic way or not. The health officer need give but little consideration to them in his plans to deal with an outbreak of bubonic plague. If people want to be vaccinated for prophylactic purposes there is no objection to complying, but the community should not be allowed to delude itself into the belief that plague may be controlled in this manner. The essential features of an antiplague campaign should be the extermination of rodents and not immunization by means of vaccines or serums."

Treatment of Leprosy, with Especial Reference to Some New Chaulmoogra Oil Derivatives.—McDONALD and DEAN (*Public Health Reports* No. 34, xxxv, 1959) take a most optimistic view of the prospects of cure in the treatment of leprosy by means of the ethyl esters of the fatty acids found in chaulmoogra oil. Their conclusions are as follows: (1) The intramuscular injection of the ethyl esters of the fatty acids of chaulmoogra oil usually leads to a rapid improvement in the clinical symptoms of leprosy. In many cases the lesions disappear, except for scars and permanent injuries, and the leprosy bacillus can no longer be demonstrated. (2) When combined with iodine, the fatty acids of chaulmoogre oil and their esters give good results; but there is no adequate experimental proof that this addition of iodine causes any increase in the effectiveness of the materials used. (3) All of the available evidence obtained from the use of fractions of the fatty acids of chaulmoogra oil indicates that the therapeutic action is due to one or more of the fatty acids of the oil or to some as yet unidentified substance associated therewith. The various methods of fractionation heretofore employed have failed to demonstrate the active agent. (4) Although conclusive evidence is not at hand, it is probable that the oral administration of chaulmoogra oil derivatives is of minor importance compared with the injections. (5) In treating leprosy, it is important to make use of all auxiliary agencies to build up and maintain bodily vigor. (6) Hypodermic injections of the ethyl esters into leprous nodules are followed by marked swelling with ultimate recession of the lesions. This is a valuable auxiliary treatment for especially resistant lesions.

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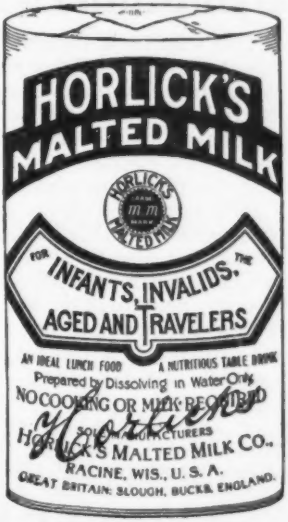
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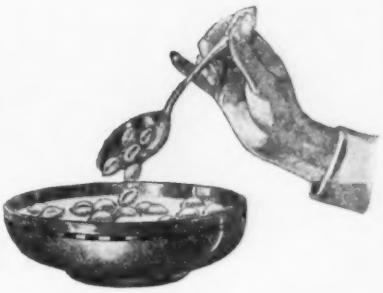

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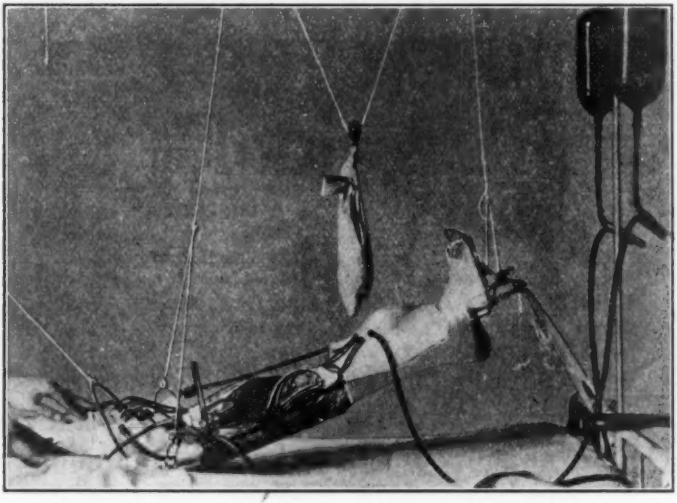

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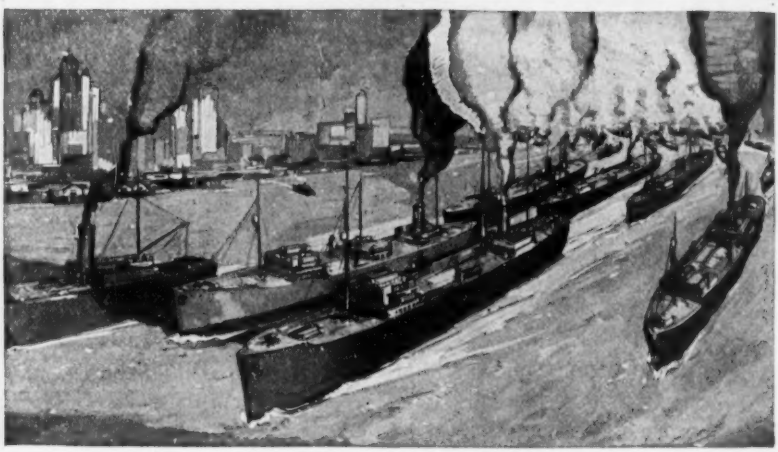

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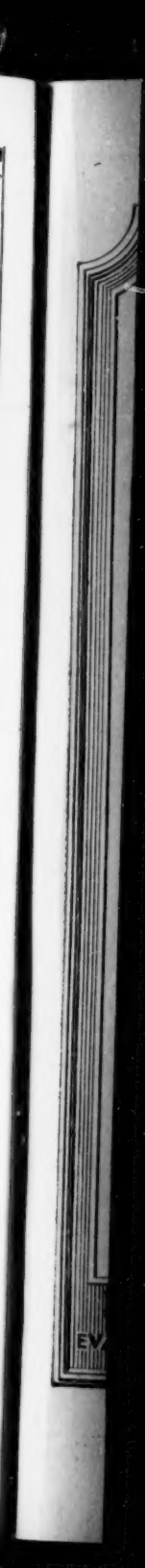

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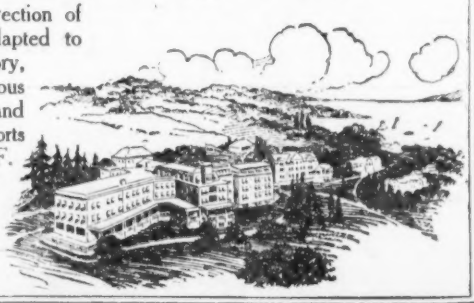

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